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BASAL BODY TEMPERATURE RECORDINGS IN GYNAECOLOGY AND OBSTETRICS

BY

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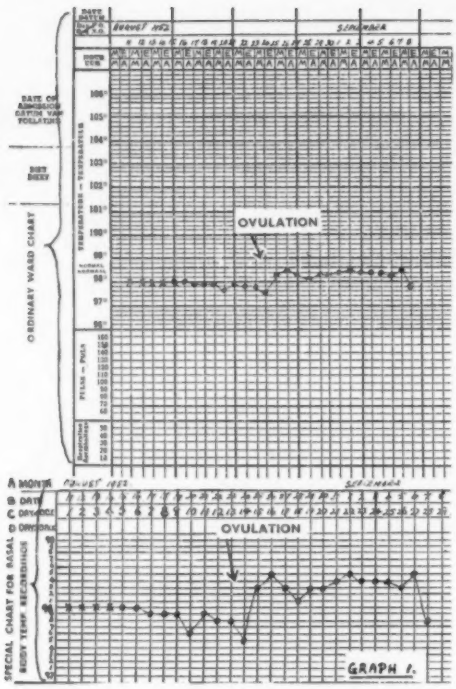
FOURTEEN years ago, when Tompkins (1944, 1945) first published his papers on basal body temperature recordings, the obvious doubt was —was this practical and was it clinical? The answer to these questions is found in our experience of the past 14 years. British literature on the subject has been very scanty; most of the writings have come from America and, although there were quite a few publications from this source between 1945 and 1950, very little has been written in the past 8 years. It was thought, therefore, that it would be useful to review the experience of 2,000 graphs which were recorded by 900 of my patients in the past 8 years to determine the present place of basal body temperature recordings in gynaecology and obstetrics.

As long ago as 1904 Van de Velde, the well-known Dutch sexologist, first pointed out that the temperature of normal women varied at different stages of the menstrual cycle; he tried to bring this to the attention of the medical profession but without success. It was not until 40 years later that Pembleton Tompkins appreciated the value and potentialities of the discovery. In 1929 Fruhinsholz observed a mild increase in temperature before menstruation and in early pregnancy. Rubenstein (1938) noted a drop in temperature round about mid-period time, which he attributed to hypothermic activity of oestrogen. It was suggested by Mocquot and Palmer (1940) that patients should take morning rectal temperatures for a few months running. Greulick and Morris (1941) proved by laparotomy that a rise in temperature meant ovulation; in 1944 and 1945 Tompkins studied the recordings in a large number of patients, devised the type of graph that is now widely used, published his findings extensively in the American literature and stressed their value in the treatment of sterility cases, in contraception, and in the diagnosis of pregnancy. Several other workers confirmed his findings (Kleitman, 1944; Davis, 1946). Halbrecht (1945) proved by endometrial biopsies that the shift in temperature meant ovulation, whereas in cases where there was no temperature change, ovulation had not occurred. Davis and Fugo (1948) and Buxton and Atkinson (1948) showed that by administering progesterone to amenorrhoeic women the temperature rose abruptly and after discontinuation of the hormone it dropped slowly. Likewise, Buxton and Atkinson (1948) demonstrated that the administration of chorionic gonadotrophin to women without ovaries did not cause a rise in temperature, but in women with ovaries there was a rise, thereby suggesting that the temperature elevation is due to progesterone. Davis and Fugo (1948) found normal temperature fluctuations in 12 women who had had hysterectomies without oöphorectomy. Cooperman (1949) described atypical recordings in two normal young girls after the menarche. Grant (1949) found that the pregnancy temperature elevation dropped as soon as the ovum died. Buxton and Engle (1950) performed 18 laparotomies soon after the rise in temperature; they examined the corpus luteum and endometrial biopsy and were not able to correlate the age of the corpus luteum or the appearance of the endometrium accurately with the temperature fluctuation. Whitelaw (1952) examined ovarian tissue removed the day of the temperature rise; in two-thirds of the cases ovulation had taken place at varying intervals up to 72 hours before the elevation; in one-third, ovulation had not taken place. The outcome of all this research is now well known.

Those who followed the original publications envisaged many problems and difficulties. Would the patients be prepared to take their temperatures every morning for weeks or months on end? In actual practice, co-operation has been remarkably good. Only 2 per cent of the patients in this series of cases did not record these charts satisfactorily. Experience has shown that any



GRAPH 1

Same cycle recorded on ordinary ward chart and usual special chart.

failure is on the part of the doctor and not the patient, the former not being prepared to go to the trouble of explaining the method. On the contrary, patients (and especially those suffering from infertility) become so keen and interested and conscientious about taking their temperatures that harm may come of it psychologically. Usually, therefore, patients are not allowed to continue with the recordings once the desired information has been obtained. The only simple thing that the patient has to know, or to learn, is how to read a thermometer. If she is so unintelligent as to be incapable of plotting the temperature recordings on a graph she can simply write down the figures and the doctor can chart them for her at the end of the cycle. A temperature is admittedly influenced by many factors but in spite of this and in spite of the human error, the readings were accurate enough to give the clinical information required (in only 8 of the 2,000 graphs was an interpretation of the graph not possible due to irregular recordings). And the final criticism—are there not better ways of telling when ovulation takes place? By endometrial biopsy the occurrence of ovulation can, of course, be diagnosed but repeated endometrial biopsy is obviously out of the question in each cycle; one can only tell in retrospect that ovulation has taken place and not the actual time of ovulation. Also, if fertilization has occurred in that cycle the pregnancy may be jeopardized. Peritoneoscopy and laparotomy are drastic procedures and can obviously only be applied to one cycle.

The method of taking the temperature is now well known. The fluctuation in temperature is slight so that the ordinary ward chart is not satisfactory. A chart producing a magnification of the small fluctuations is used (this is clearly shown in Graph 1). The temperature must be basal and any "cold" illness, discharge, bleeding or other symptoms of significance must be noted. In order to facilitate the taking of the temperature special thermometers have been devised with magnifications of the spaces—this is not necessary and the ordinary clinical thermometer is perfectly adequate and was used by all our patients.

Cases Demonstrating the Uses of the Graphs

Graph 2 shows normal ovulation in a woman who is menstruating normally and also shows that oral temperatures are as satisfactory as rectal temperatures.

Graph 3 are the recordings in a girl before puberty.

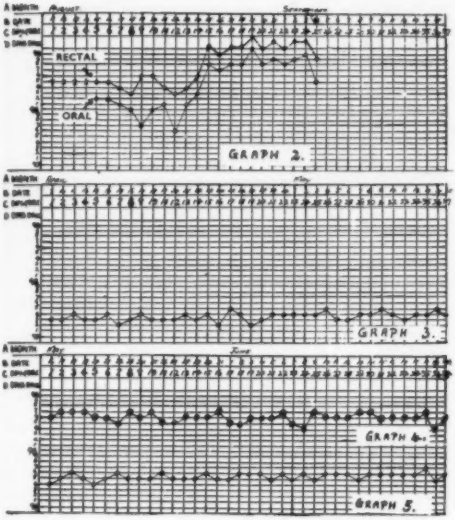
Graph 4 are the recordings in a woman after the menopause.

Graph 5 is the chart of a man aged 38 years.

The Uses of the Normal Chart

A. Contraception

Most authors agree that the ovum lives for 48 hours or, very likely, less than that (Knaus, 1929; Allen *et al.*, 1930). Once the temperature has



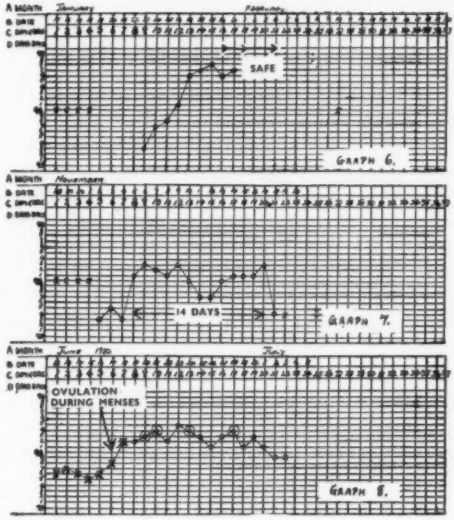
GRAPH 2
Oral and rectal recordings in normal cycle.

GRAPH 3
Recordings in a girl before puberty.

GRAPH 4
Recordings in a woman after the menopause.

GRAPH 5
Recordings in a man aged 38 years.

been up for 48 hours, therefore, conception is not possible and intercourse can take place for almost 2 weeks of the month with complete confidence that conception will not occur. In fact that is the most scientific method of birth control. All other methods of birth control are crudely scientific, being mechanical or chemical. This method is reliable no matter how irregular the cycle is. The Ogino-Knaus method, Minerva Calendar, and other methods of applying the "safe period" depend on regular cycles—they are particularly unsafe when one or more cycles suddenly become irregular. This method does not entail as much trouble as might be thought. For example, in a 28-day cycle, she need only start taking her temperature a few days after the end of menstruation and continue until the temperature has been up for 48 hours—there is no point in continuing for the rest of the cycle. This is demonstrated by Graph 6. This method is permissible by the Roman Catholic Church, which does not allow birth control. The question arises as to whether there is a "safe period" before ovulation. There is in most cases but this is not at all as certain as in the post-ovulatory phase. There are three possible sources of error. It is particularly unsafe when there is a short cycle and thus an early ovulation soon after menstruation (Graph 17 demonstrates this point). Secondly, a woman with a usually regular 28- or 30-day cycle might suddenly have a short period and thus ovulate soon after menstruation, as shown in Graph 7. Thirdly, the sperm may possibly live in the cervix and other parts of the genital tract for some days. Thus, when ovulation takes place several days after intercourse, spermatozoa may still be available from that intercourse for fertilizing the ovum. In certain animals the sperms retain their ability to fertilize



GRAPH 6
Birth control.

GRAPH 7
Irregular short cycle.

GRAPH 8
Infertility. Ovulation during menstruation.

the ovum for a considerable length of time. The bat, for example, has coitus in autumn but ovulation and fertilization only occur in the following spring. The queen bee, after having had coitus, can lay fertilized eggs for years. In the rabbit and certain other animals ovulation is precipitated by coitus—investigation of many hundreds of these graphs indicates that this does not occur in women. Likewise, these graphs show that ovulation never occurs twice in one cycle.

B. Infertility

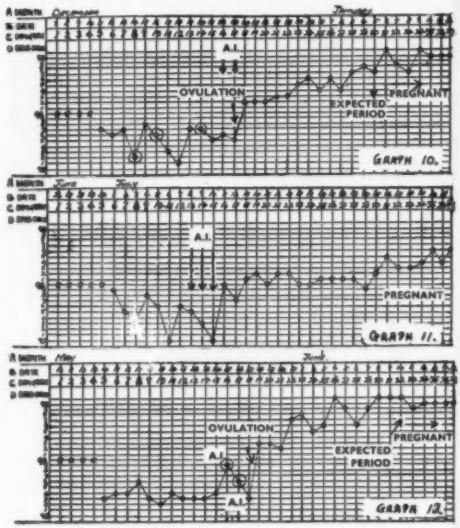
The graph will obviously help to diagnose those cases that are not ovulating; this will be discussed later. Where ovulation is taking place normally, the graph can help conception under the following circumstances:

(1) *Ovulation during menstruation.* It will show the patient the optimum time for attempts at conception. Graph 8 indicates an infertility patient who had a regular 21-day cycle and her periods always lasted for 7 days. She obviously ovulated on the last day or two of menstruation and her inability to conceive was due to abstinence at this time. The patient was advised to have intercourse during menstruation and she became pregnant within 3 months.

(2) *Infrequent ovulation.* In irregular cycles with infrequent menstruation the time of ovulation is obviously important, especially if a woman only ovulates, and therefore only menstruates, once in 2 to 3 months—she has only one or two fertile days in 2 or 3 months. The graph may be of value (Graph 21) in indicating to her the optimum time for attempts at fertilization.

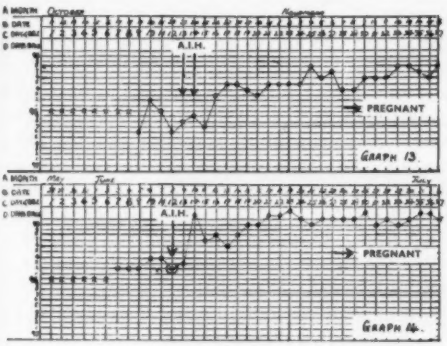
(3) *Low sperm count.* If the sperm count is low, for example in the order of 40 million, abstinence can be practised until ovulation so as to build up a maximum store of available spermatozoa.

(4) *Artificial insemination.* In both types of artificial insemination (that is, using a donor's semen or a husband's semen) the temperature graph is invaluable, indicating the day or days for the insemination. I do not carry out artificial insemination with a donor's semen but Graphs 10, 11 and 12 are those of patients of mine who had conceived following this procedure, which



GRAPHS 10, 11 AND 12
Artificial insemination (donor).

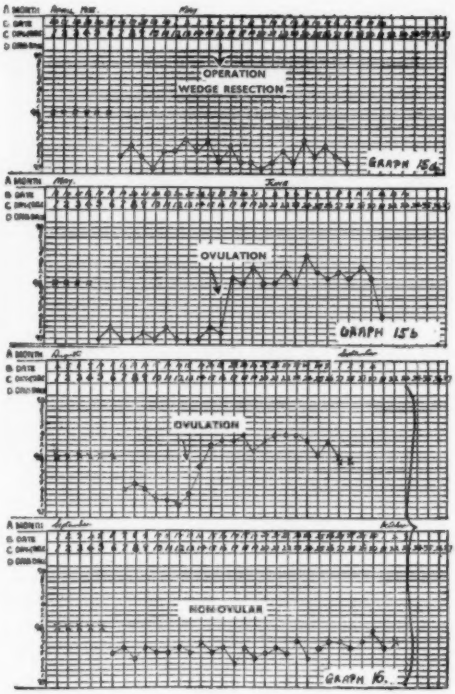
was carried out by a friend and colleague. Most doctors are not averse to using artificial insemination with the husband's own semen. According to the literature this form of insemination is only indicated for abnormalities in the husband where the sperm count is not subnormal but where he is incapable of depositing semen in the vagina—for example, hypospadias. No references to indications in the wife have been seen in the literature. Two patients are presented with gynaecological indications, who were treated with success. Graph 13 is that of a patient who was complaining of 9-years infertility. She had a normal uterus, shown clinically and verified by hysterosalpingogram. There was no cervix just a dimple at the vault of the vagina, with a small opening leading into the uterine cavity. Her husband was normal. His sperms were injected through that opening with a syringe and she became pregnant. Graph 14 shows the temperature recordings of a woman whose complaint was primary sterility of 4-years duration. The husband's sperm count was normal. She was ovulating regularly and her tubes were patent. The hysterogram, however,



GRAPHS 13 AND 14
Artificial insemination (husband).

showed an abnormally long cervix (Film 1). Artificial insemination with her husband's sperms, injecting them through the cervix, was successful.

(5) *Absence of ovulation.* Absence of ovulation is not nearly as common a cause of sterility as are tubal factors, faults in the sperm picture and gross pathology in the genital tract. This is fortunate because the treatment of non-ovulation is usually difficult and unsatisfactory. The following two graphs demonstrate cases of failure of ovulation (Graphs 15a and 15b). A nursing sister at the Port Elizabeth Hospital complained of sterility of 6-years duration. On investigation the sperm analysis was normal, her tubes were patent, and there was no gross pathology in the genital tract. She was, however, a tall and masculine type of woman, with hirsutism and both her ovaries were enlarged and cystic. The graph as seen here shows a failure of ovulation. Following an examination under anaesthesia and a diagnostic curettage the diagnosis was made of the hyperthecosis syndrome. On the 9th May, 1955, a wedge resection was carried out on both ovaries. As can be seen from the graph, she started ovulating the next month and has continued to ovulate regularly ever since. She became pregnant a year later and her pregnancy graph is available; unfortunately she aborted at 10 weeks, but is still hoping for a successful pregnancy. Graph 16 is that of a patient who



GRAPH 15a
Non-ovular cycle before wedge resection of ovaries.

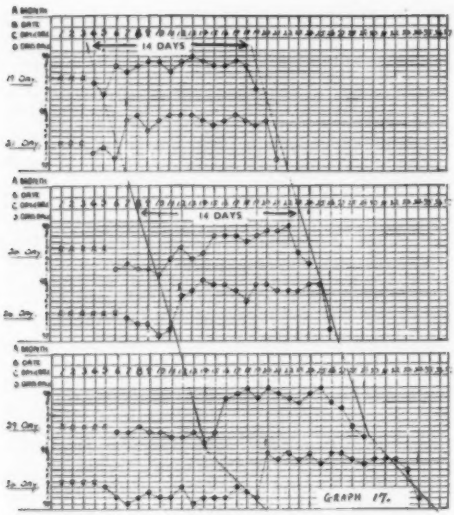
GRAPH 15b
Ovulation in the month following wedge resection operation.

GRAPH 16
Infrequent ovulation at the climacteric.

married at the age of 43 years and was very keen on a family. All fertility factors were normal except ovulation, probably due to the impending menopause.

C. Irregular Menstruation

This is a common condition. The condition is difficult to rectify. The patient does not know when she is going to menstruate and does not know when she is and when she is not pregnant. Treatment to establish regular cycles is difficult.



GRAPH 17
Post-ovulation phase always 13–15 days.

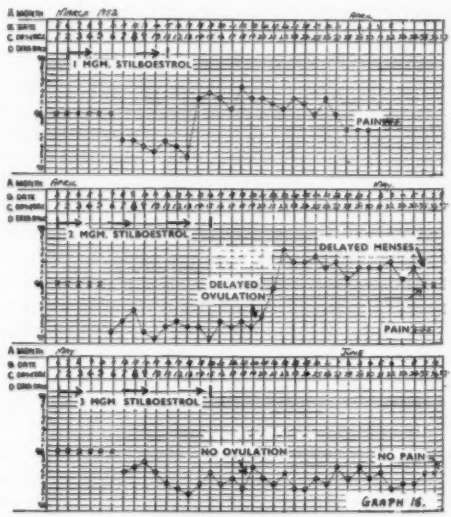
A satisfactory way of dealing with this situation is to advise her to record her basal body temperature. Thereby all the difficulties are cleared up because no matter how long or short the phase is before ovulation—one day or three months—once ovulation takes place the post-ovulation phase is invariably 13 to 15 days. This is clearly demonstrated by Graph 17. The recordings will therefore show the patient when her next period will come on and when she is pregnant. This is particularly useful because many of these cases are associated with habitual abortion. As soon as the graph indicates that the patient is pregnant, rest and other treatment can be instituted immediately.

D. Dysmenorrhoea

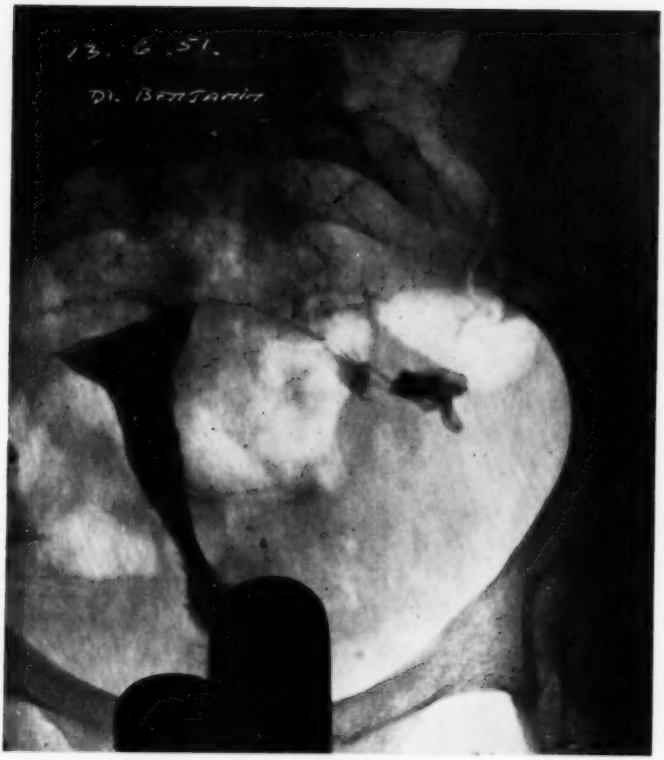
The treatment of spasmodic dysmenorrhoea is often difficult and unsatisfactory but it is well known that by inducing non-ovular cycles the dysmenorrhoea can be relieved. The method may be used therapeutically in one or more cycles; it may also be employed as a diagnostic procedure when there is doubt as to whether the dysmenorrhoea is spasmodic. This result can be achieved by administering oestrogens in the first half of the cycle. The aim is to prescribe the smallest dose of oestrogen which will inhibit ovulation and in order to achieve this temperature graphs are of help. Graph 18, taken by a patient with severe dysmenorrhoea, shows clearly the effect of such oestrogen therapy. If small doses are given there will be no effect on ovulation or menstruation; if a somewhat higher dose is given, ovulation will be postponed, but will occur, and thus menstruation will be postponed but will still be painful; if the correct dosage is given, ovulation will be inhibited and a painless bleeding will result.

E. Endometriosis

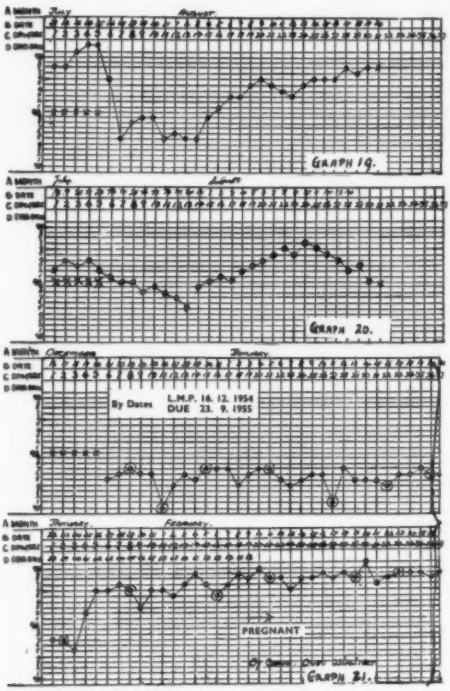
Endometriosis is a notoriously difficult condition to diagnose at times. Latent, undiagnosed endometriosis is not infrequently a cause of sterility where other fertility factors are normal. In 1947 Jeffcoate pointed out that in many cases of endometriosis pyrexia occurred at the time of menstruation. This is understandable because at each menstruation there is virtually the formation of a haematoma in the ovaries, uterine wall, or pelvic peritoneum. Jeffcoate did not



GRAPH 18
Treatment of spasmodic dysmenorrhoea with oestrogens



FILM 1



GRAPH 19
Pyrexia during menstruation—endometriosis.

GRAPH 20
Pyrexia during menstruation—endometriosis.

GRAPH 21
Postmaturity.
By dates due on 23rd September, 1955.
By chart due on 23rd October, 1955.

actually suggest the following procedure but, since in most of these cases the pyrexia may pass unnoticed, all unexplained sterility cases were told to take their temperatures during menstruation as well as at other times of the cycle. Cases of unexplained sterility due to latent endometriosis were thereby diagnosed, as shown by these two examples.

Graph 19 is that of a patient who complained of sterility of 4-years duration. Nothing abnormal was found clinically, the sperm analysis was normal, her tubes were patent and she was ovulating, although with not quite the typical pattern. She was told to take her temperature at the time of menstruation as well as during the rest of the cycle. As can be seen from the graph she had a definite pyrexia at menstrual time. Laparotomy proved the presence of small chocolate cysts in both ovaries and endometriomatous deposits in both utero-sacral ligaments as well as in the pelvic peritoneum.

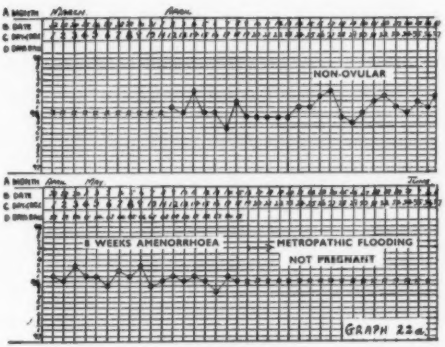
Graph 20 is another example confirming the pyrexia at menstrual time in a case of endometriosis. In this case the endometriosis was situated in a laparotomy scar.

F. Abnormalities of Pregnancy

Basal body temperature recordings can also be of value in obstetrics, as demonstrated by the following patients:

Postmaturity. In women with irregular cycles it is difficult to calculate the duration of pregnancy by basing it on the date of the last menstrual period—conception may have occurred later, i.e., during a period of amenorrhoea. If the patient were on an ovulation graph—and many of such patients were on graphs because sterility is often associated with irregular cycles—then the diagnosis can be made accurately, as is shown by Graph 21.

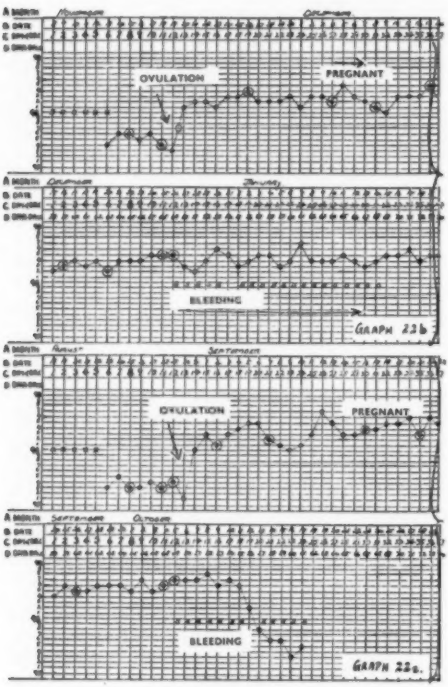
Bleeding in early pregnancy. One of the commonest clinical problems one encounters in pregnancy is vaginal bleeding in the early months. This usually represents a threatened abortion. However, especially if the bleeding and



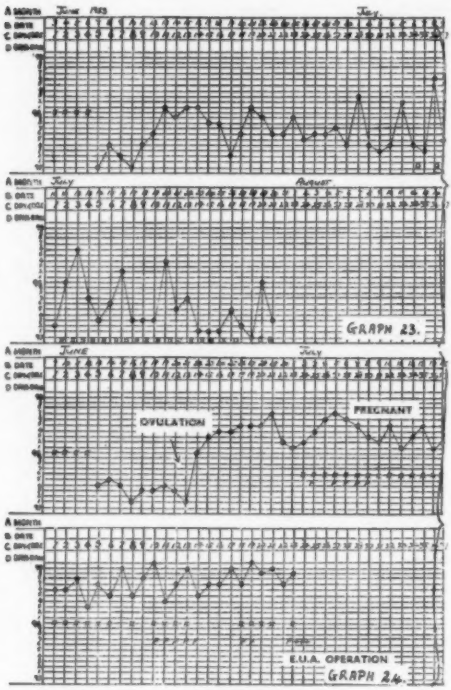
GRAPH 22a
Metropathia.

brown discharge continues, the problem is whether this is a pregnancy at all and, if it is a pregnancy, whether the ovum is alive or is dead. The graph clarifies the issue. Graph 22a shows a case of amenorrhoea, followed by bleeding; there is no ovulation and the case is one of endocrine bleeding and not of pregnancy.

Graph 22b shows another case of amenorrhoea followed by bleeding. This is a pregnancy, the elevated temperature indicating that the ovum was still alive and the continuation of the treatment worthwhile. Graph 22c shows yet another case presenting with amenorrhoea, followed by bleeding, but the temperature dropped soon after the bleeding. The diagnosis is therefore one of a missed abortion with death of



GRAPH 22b
Threatened abortion.
GRAPH 22c
Missed abortion.



GRAPH 23
Hydatidiform mole.
GRAPH 24
Ectopic pregnancy.

the ovum. It would be pointless trying methods to conserve this pregnancy.

Hydatidiform mole. Graph 23 looks rather peculiar but it is unique because such a recording has not been encountered in the literature. This patient had 5-weeks amenorrhoea followed by continual brown discharge and slight bleeding. The graph was so atypical that a diagnosis could not be made. The temperature seemed to swing up and down to a marked degree. This was the first case we had had on a graph where the diagnosis of pregnancy was not certain. On the 76th day, i.e., after 11-weeks amenorrhoea, the patient aborted—a hydatidiform mole.

Ectopic pregnancy. Graph 24 is also unusual and must be a rare recording. The patient had

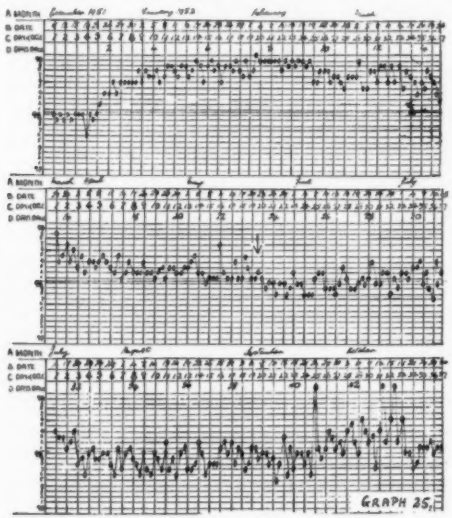
irregular, intermittent bleeding, at times profuse, but the temperature did not drop. From the amount of bleeding and the pain and the size of the uterus, one would have expected the ovum to have died and the temperature to have dropped. Further investigation, and operation, showed that she had an ectopic pregnancy.

G. Graphs for Research Purposes

So far we have dealt with the actual everyday clinical applications of the graph. It was decided over the past few years to investigate certain basal temperature recordings that had not been done before, or at any rate not to any extent.

Temperature Pattern Throughout the Entire Pregnancy

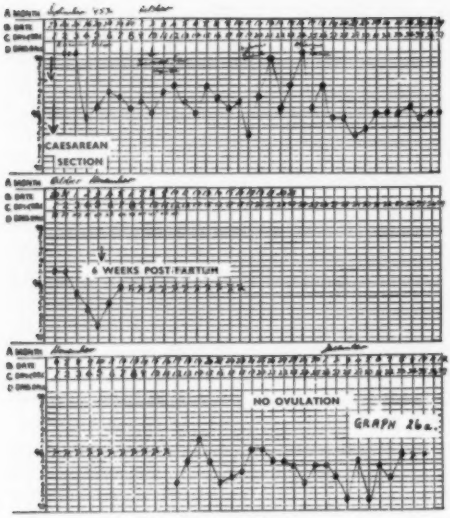
Six patients, mostly nursing sisters and doctors who were only too pleased to co-operate, carried out their basal body temperature recordings throughout pregnancy. One of the sisters, who was originally treated for infertility, recorded her temperature throughout both her pregnancies as well as before, after, and between the pregnancies continually for five years (this she did voluntarily and happily and we were quite sure that there were no adverse psychological effects). The recordings throughout 7 entire pregnancies were therefore made and one of these is shown in Graph 25. The graphs are interesting. In all cases the temperature remained high until the 13th to 14th week. The temperature then begins to drop from the 13th week but it does not reach the pre-ovulation level until much later. In 3 cases the temperature dropped to the pre-ovulation level at the 23rd to 24th week, in 2 cases at the 33rd week and then in 1 case at the 36th week and in 1 case only just prior to the onset of labour. This is all very interesting but it is difficult to explain. The shift in temperature during the menstrual cycle has been abundantly proven to be due to progesterone and to no other hormone or combination of hormones (Davis and Fugo, 1948; Buxton and Atkinson, 1948). In pregnancy the secretion of progesterone continues to increase until it reaches the maximum just before the onset of labour—it would therefore be expected that the temperature would remain elevated and even rise higher and higher until the onset of labour, but this does not occur, as shown by the graphs. The temperature pattern may possibly correspond to the behaviour of the progesterone of the corpus luteum and not of the placenta. This raises the interesting question as to whether the progesterone from the corpus luteum is different from that from the placenta. On the other hand the explanation may be found in the hypothermic action of oestrogen.



Graph 25
Basal temperature recordings throughout entire pregnancy.

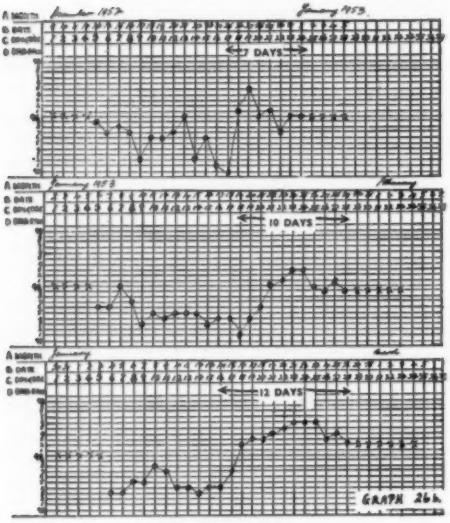
Temperature Pattern and Ovulation in the First Few Months After Pregnancy

When does a patient first ovulate after delivery? The same patient who made the recordings throughout her 2 pregnancies continued taking her basal body temperature immediately after delivery without a break. Her graphs show clearly when she first ovulated after delivery. Graphs 26a and b, show the recordings after the first baby in 1952. She first menstruated 6 weeks after delivery and this was not preceded by ovulation. Her next cycle, a 33-day one, was also non-ovular. In the third



GRAPH 26a

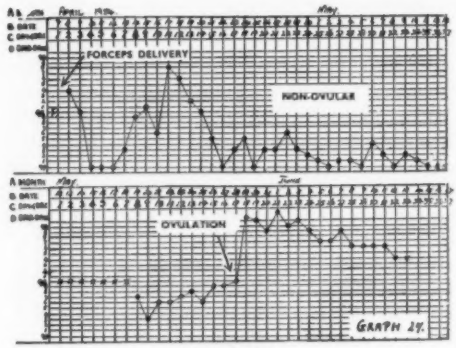
Recordings immediately after delivery.



GRAPH 26b

Recordings of 26a continued.

cycle there appeared to be a poor corpus luteum, with a post-ovulatory rise of only 7 days. The 4th cycle showed a post-ovulatory phase of 10 days. The 5th cycle showed a post-ovulatory phase of 12 days, and it was only in the 6th and subsequent cycles that normal ovulation took place with the usual 14-day rise of temperature after ovulation. In no other graphs was a variable post-ovulation phase like this encountered. Graph 27 shows the recordings after the second baby in 1954. She first menstruated 5 weeks after delivery, a non-ovular cycle. The very next cycle, however, was an ovulatory one with a normal post-ovulation rise in temperature of 14 days.



GRAPH 27

Recordings immediately after delivery.

OVULATION IN YOUNG GIRLS JUST BEFORE AND SOON AFTER THE MENARCHE

For a long time it has been thought that young girls do not ovulate for 2 or 3 years after the menarche, the menstruation being non-ovulatory. This has, however, been questioned (Novak, 1944; Shippel, 1955). The former actually states that there is no doubt that in many, and probably a great majority of, girls ovulation occurs from the *first* menstrual cycle and that the very first menstrual bleeding is preceded by ovulation. Shippel (1955) states that if this were not the case the hyperthecosis syndrome would be an extremely common condition because his theory as to the pathogenesis of the condition is

the occurrence of non-ovulatory cycles over a period of time. I felt that one could settle the issue once and for all by the use of basal body temperature recordings. My niece, aged 12 years, began to menstruate a few months ago. She and two of her friends (in a similar physiological state) were happy to take their temperature recordings (all the necessary precautions being taken to prevent any psychological reaction). Two of them started menstruating and their very first menstrual cycles were preceded by ovulation.

Summary and Conclusions

(1) Basal body temperature recordings have been used in clinical gynaecology for about 12 years. It was considered timely to take stock of the subject and determine its present place in obstetrics and gynaecology. This was done by a study of 2,000 such graphs recorded by 900 patients and by a consideration of previous literature on the subject.

(2) It is shown that this is a practical procedure and that many of the anticipated difficulties, such as inaccuracy of records and lack of co-operation by patients, are not great. An important disadvantage is the psychological one, especially in infertile patients, who may become too introspective and obsessed with their recordings. It is considered inadvisable to allow many of these patients to continue such recordings after the desired information has been obtained.

(3) Basal body temperatures are of value as a method of contraception, in cases of irregular menstruation, in the treatment of spasmodic dysmenorrhoea and in the diagnosis and treatment of infertility. (Indeed, in some patients in this series the cause of the infertility could not have been detected without the aid of such graphs.)

(4) It has been shown that certain cases of endometriosis which would otherwise have been overlooked may be detected by this method.

(5) These temperature graphs can be useful adjuncts in assessment of certain abnormalities in obstetrics, especially bleeding in early pregnancy, and postmaturity. A few rare recordings (cases of hydatidiform mole and ectopic pregnancy) are presented.

(6) Basal body temperature recordings have helped to clear up certain questions in gynaecology that have been controversial in the past, including:

(*a*) when ovulation first takes place after childbirth,

(*b*) whether young girls ovulate before, at, and soon after the menarche,

(*c*) whether coitus can stimulate ovulation in women,

(*d*) whether ovulation can occur twice in one menstrual cycle.

(7) The temperature patterns throughout 7 entire pregnancies are shown and the interpretation of these findings is discussed.

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OBSTRUCTED LABOUR

A Series of 320 Cases Occurring in 4 Years in a Hospital in Southern Nigeria

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EXCEPT in isolated cases, obstructed labour is rarely encountered in present-day British obstetric practice. Chassar Moir (1946, 1947) has emphasized that, though until recently most abnormalities were dealt with as they arose, today, and this is especially true of those conditions causing obstructed labour, they are detected and can be treated as planned procedures. Because of this the methods used for delivery have resolved into Caesarean section, a simple forceps extraction or a normal delivery.

Dystocia due to pelvic tumours, gross foetal and pelvic abnormalities which comprise the majority of reports of obstructed labour in British and American literature, is rare here and relatively unimportant as few diagnostic or technical problems are presented unless the woman is *in extremis*. The greatest problem in Nigeria is the prevention and treatment of obstruction due to cephalo-pelvic disproportion at the pelvic brim, of which all degrees are seen from early obstruction with the foetus still alive, to the infected exhausted woman, the foetus dead, the uterus in tonic contraction and rupture imminent. Most of the patients in this series were seen late in the second stage of labour with established obstruction and immediate delivery imperative. They comprise only a small proportion of the total admissions with gross disproportion or malpresentations, as the majority were diagnosed before or early in labour and were delivered before obstruction could develop.

MATERIAL

During the 4 years from April, 1953 to 1957, 320 patients have either been admitted in obstructed labour or labour has become obstructed when in hospital. Hospital deliveries during this period totalled 17,230 (14,361 booked and 2,869 emergency cases) giving an incidence of obstructed labour of 1 in 189 deliveries. The patients were unselected, all women demanding admission being accepted.

Obstruction in labour is the largest individual factor in both maternal deaths, accounting for 44 (27·2 per cent) of 162 deaths, and in stillbirths, causing 198 (18·8 per cent) of 1,052 stillbirths.

Though any woman who is unable to deliver herself by natural means may be said to be in obstructed labour, this definition would include a large number delivered easily by simple methods. With the exception of one patient with cervical stenosis, no case appears in this series who had not been in the second stage of labour, with membranes ruptured for varying periods of from 1 to 36 hours, and in the case of cephalic or breech presentations, with the presenting part still above the pelvic brim at the time of delivery.

LOCAL CONDITIONS

These patients were all delivered in Adeoyo Hospital during its temporary occupation by

University College staff. This small hospital provided 46 maternity beds for the town and rural district of Ibadan, with a population of about 750,000, mainly indigenous Yorubas, but with a number of Ibos from Eastern Nigeria and other tribal groups. The available hospital beds were grossly inadequate, even though only a small proportion of the population are delivered in hospital. Overcrowding and paucity of nursing and medical staff, especially at the onset of this survey, accounted for a number of these cases who, owing to lack of adequate supervision, actually obstructed in the labour ward.

As childbirth is not regarded as an abnormality, but as a normal physiological process, many women still prefer to be delivered at home without skilled assistance and come into hospital only as a last resort. Transport difficulties, especially at night, long distances and inaccessibility of many of the villages add considerably to the delay in admission.

Pregnancy and Labour in Nigerian Women

In both primigravidae and multigravidae engagement of the foetal head rarely occurs until the end of the 1st or onset of the 2nd stage of labour, and appears to be uninfluenced by rupture of the membranes. This late engagement does not prolong labour, for seldom is the 1st stage longer than 12–18 hours or the 2nd stage 10–30 minutes. Except among sophisticated patients, introspection and fear play little part in prolonging labour, and delay of over 24 hours is almost invariably due to disproportion.

One factor in this late engagement of the head is the steep inclination of the pelvic brim, which is almost vertical in some cases and is compensated by a marked lumbar lordosis. No radiological study has yet been made of the Nigerian pelvis, but on clinical examination it is shallow and in the majority of women the promontory of the sacrum can easily be reached. This corresponds with the findings of Sibthorpe and Allbrook (1958) on the Bantu pelvis. Many women are small; among booked patients 24·5 per cent were below 5 feet, 47·5 per cent between 5 feet and 5 feet 2 inches and only 27 per cent taller than this. The smallest patient in this series was 3 feet 6 inches tall, an achondroplasic dwarf, who was admitted late in the 2nd stage of labour with a ruptured uterus, though her first two babies had been delivered normally. Fortunately, the foetal size is commonly small, the average baby weighing between 6 and 6½ pounds.

The majority of labours at home or in hospital are rapid and uncomplicated; the woman works up to the last minute and resumes work almost immediately. Rupture of the membranes is taken as a sign of full dilatation of the cervix and she commences to bear down. This has never been observed to predispose to rupture of the uterus as has been suggested by Lavery (1955), though the cervix and vulva may become oedematous and the foetus distressed. In a home confinement, if delivery is not accomplished within a reasonable time, the relatives or native doctor may resort to very active and inexpert measures, and various "native medicines" are applied externally especially to the vulva or taken orally in large quantities, thereby adding considerably to the anaesthetic hazards when she is eventually admitted. The majority of these "medicines" are toxic and strongly aperient, but the presence of an oxytocic principle has not been proved.

Parity

Of the 320 patients 31·3 per cent were primigravidae, compared with an almost identical figure for all hospital deliveries of 32·1 per cent, and a comparison of the causes and results of obstruction in primigravidae and multigravidae shows great similarity except in the incidence of ruptured uterus and transverse lie. There is, however, a marked difference between booked and emergency patients regardless of parity, as the woman who has been attending the Antenatal Clinic, if in trouble, tends to come into hospital earlier, often before full dilatation of the cervix and before obstruction has developed.

Premature labour due to malaria, anaemia, malnutrition or other illness, or to multiple pregnancy is so common that many small multigravidae have technically untried pelves, and deliver one or more babies successfully until a normal sized child, especially if the occiput is posterior, causes obstruction.

Previous Obstetric Abnormalities

Forty-one women gave a history of abnormalities in previous deliveries, and in 32 the infant was stillborn. Five had been delivered by craniotomy, one woman on two occasions, and 2 were found to have vesico-vaginal fistulae dating from previous obstructed labours. These figures are probably an underestimation as women here tend to suppress past catastrophes.

After labour became obstructed again in the 2nd stage, 29 women were delivered by Caesarean section with the loss of one baby. Four patients were admitted after rupture of the uterus, with one maternal death. Destructive operations were required to complete delivery on 6 occasions, and high forceps were applied twice. The following case history illustrates the difficulty in convincing patients of the value of hospital treatment.

Molundi, aged about 20 years, a primigravida, was admitted in 1954 in obstructed labour, after 5½ hours in the second stage and with the foetal head unengaged. She was delivered by craniotomy and a twisted solid ovarian carcinoma removed 3 days later. Her height was 4 feet 6 inches and the foetus weighed 5 pounds 5 ounces. She reported again in 1955 when 26-weeks pregnant and attended the clinic fairly regularly, but, in spite of her past experiences, appeared in obstructed labour after 5 hours in the second stage, the head unengaged and the occiput posterior. She was delivered of a live 5 pounds 6 ounces baby by Caesarean section. No metastases were found.

Causes of Obstructed Labour

I. Cephalo-Pelvic Disproportion at the Pelvic Brim

Disproportion between the pelvic brim and the forecoming foetal head presenting by the vertex, accounted for 67 per cent of all cases of obstruction and 70 per cent of the maternal deaths.

Table I
Diagnosis

Diagnosis	Booked Cases	Emergency Cases	Total
Cephalo-pelvic disproportion	76 (5)	139 (26)	215 (31)
Malpresentation and compound presentations	15	61 (9)	76 (9)
Locked twins	3	4	7
Contraction ring	1	1	2
Cervical or vaginal stenosis	1	2	3
Impacted shoulders	0	7 (3)	7 (3)
Foetal abnormalities	1	9 (1)	10 (1)
	97 (5)	233 (39)	320 (44)

Maternal deaths in parenthesis.

Table II
Treatment

Treatment	Booked Cases	Emergency Cases	Total
Caesarean section	62 (2)	46 (2)	108 (4)
Forceps delivery	5 (2)	22 (1)	27 (3)
Destructive operations	18	75 (7)	93 (7)
Laparotomy (ruptured uterus)	5	55 (19)	60 (19)
Breech extraction	3	12 (1)	15 (1)
Delivery of locked twins	3	4	7
Died undelivered	1 (1)	9 (9)	10 (10)
	97 (5)	223 (39)	320 (44)

Maternal deaths in parenthesis.

Obstruction resulted from a combination of factors: small pelvis, an occipito-posterior position, and in a few cases a foetus of more than average size.

These patients can be divided into two distinct groups depending on the time of admission to hospital. Sixty-seven (31 per cent) were admitted during the first stage of labour and 148 (69 per cent) in the second stage. In the first group are women in whom it was considered that the degree of disproportion was minor enough to justify a trial of labour. After one or more hours in the 2nd stage with ruptured membranes and the head still unengaged, and when it was obvious that moulding would not enable the head to pass through the brim, the majority (56) were delivered by Caesarean section, or, if the foetus was dead, by craniotomy or forceps. As the head rarely engages before the second stage of labour, a considerable degree of skill is required in borderline cases to forecast the outcome of labour. Judged by results it is evident that in all cases the degree of disproportion was greater than was estimated, and a section done earlier would have reduced the high foetal and maternal mortality. Fourteen (20·8 per cent) of these babies were either stillborn or died within a few days as the result of asphyxia or cerebral damage. The 3 maternal deaths were all due to sepsis; the 2 cases of ruptured uterus both survived.

The second group of 148 women presented a much more formidable problem. The majority were in advanced obstructed labour, after many hours in the 2nd stage. Such a woman was febrile, dehydrated and shocked, the severity of the circulatory failure depending on the length of labour, degree of infection and the presence of uterine rupture. The uterus was in tonic contraction, tense, tender and the foetal heart rarely heard. In all these women the head was unengaged though, frequently, because of the shallow pelvis, the caput was visible at the vulva. The division between the upper and lower segments, often at the level of the umbilicus, was accentuated by a distended oedematous bladder, and the head was so firmly wedged in the brim that a catheter could rarely be passed without dislodging the head. In most cases of advanced obstruction and in all cases of uterine rupture there is some degree of haematuria. A fistula was already present in a few cases, probably from trauma as the slough of pressure necrosis takes some days to separate.

Immediate delivery is imperative, after essential preliminaries such as resuscitation, obtaining compatible blood, emptying the stomach and the administration of antibiotics and tetanus antitoxin. Caesarean section was performed 41 times, never when the foetus was already dead, yet 10 infants were stillborn. Though the foetal heart sound may be present at the onset of the operation, a severely asphyxiated foetus rarely survives even the most expert operation, or if born alive may die later from cerebral damage. On a number of patients with doubtful foetal heart sounds, an attempt was made to deliver by high forceps rather than perforate a baby which might be alive. In all only 37 (25 per cent) of these babies survived, 31 being delivered by Caesarean section and 6 by forceps.

Of the remaining women, 40 were delivered by craniotomy, 35 were operated upon for rupture of the uterus and 5 died undelivered.

Craniotomy is generally both easier and quicker than Caesarean section. The method used here is to perforate the head with a sharp perforator, evacuate the maximum amount of brain, grasp the bone edge with Morris's forceps and deliver by steady traction and slight rotation. On no occasion was it necessary to crush the skull with a cranioclast, a much more difficult operation with considerably more danger of maternal injury. Following delivery there is generally a gush of offensive thick meconium, gas, blood and urine. The uterus is immediately explored, and a rupture dealt with if present.

II. Transverse Lie

Forty-eight cases of obstruction due to impacted shoulder presentation occurred, all but one in multigravidae. The lax multiparous uterus was the most important aetiological factor, but in addition 11 of the babies were second twins and placenta praevia was present in 5 cases. The one primigravida was a small woman with a generally contracted pelvis. Many of the babies were small, 45 per cent weighing less than 5½ pounds.

Apart from 5 patients admitted in the first stage of labour, the malpresentation being unrecognized until obstruction had developed, the remaining 43 women were all admitted during the second stage, the majority late in labour with the uterus in tonic contraction clamped round a dead foetus making any operation but decapitation dangerous and technically almost impossible. Thirty-four patients had on admission been in the second stage for more than 4 hours, 26 more than 8 hours and 18 over 12 hours. Twenty-five women were delivered by decapitation performed either with a sharp hook, long scissors or a Blond Heidler saw. In 9 instances, mostly to deliver a second twin or triplet, it was possible to perform an internal version and extraction, with craniotomy of the aftercoming head in 2 cases, one foetus being hydrocephalic. A Caesarean section was done once only, on a patient on whom a misdiagnosis of rupture of the uterus was made. This woman admitted after 8 hours in the second stage of labour, had obstructed in a previous pregnancy and sustained a large vesico-vaginal fistula which had been treated by uretero-colic anastomosis.

The remaining 12 patients were admitted with the uterus ruptured. Three were of interest in that the placenta had been delivered 15 hours, 9 hours and 12 hours before admission. The first two were exsanguinated and died during or soon after delivery, but the third survived, though at laparotomy a foetal arm was missing, apparently pulled off in attempts at delivery prior to admission, this trauma probably rupturing the uterus.

The foetal and maternal mortality were higher in this than in any other aetiological group, partly because of late admission to hospital. There were 7 maternal deaths (17·9 per cent), all but one due to rupture of the uterus. The foetal mortality was 89·5 per cent, only 4 babies surviving.

III. Foetus Partially Delivered on Admission

Three conditions come under this heading:

(1) Locked twins, 7 cases, 0 maternal deaths.

(2) Impacted shoulders, 7 cases, 3 maternal deaths.

(3) Retained aftercoming head, 6 cases, 2 maternal deaths.

(1) *Locked Twins*

In the last 4 years, with 17,230 deliveries and 980 sets of twins, the incidence of locking was 1 in 2,461 total deliveries and 1 in 140 twin

Table III

Locked Twins

Case No.	Parity	Condition on Admission	Treatment	Result to Child	Birth Weight	
					Pounds	Ounces
1	Para-1	Locked 11 hours. Eclampsia	Perforation 2nd head, both extracted	Stillbirth Stillbirth	5 5	0 6
2	Para-1	Locked 16 hours	Perforation 2nd head, both extracted	Stillbirth Stillbirth	4 3	10 6
3	Para-0	Locked 1½ hours	Perforation 2nd head, both extracted	Stillbirth Stillbirth	5 4	6 1
4	Para-0	Locked 12 hours	2nd head disimpacted, 1st extracted, 2nd delivery by forceps	Stillbirth Stillbirth	3 4	12 12
5	Para-2	Locked 11 hours. V.V.F.	1st decapitated Craniotomy 2nd head	Stillbirth Stillbirth	7 5	0 4
6	Para-0	Locked ½ hour	1st decapitated, head disimpacted, 2nd forceps	Stillbirth Alive	4 5	13 9
7	Para-1	Locked 1 hour	2nd disimpacted, breech extraction and spontaneous delivery	Stillbirth Stillbirth	4 4	7 4

deliveries, compared with the figure of 1 in 90,000 deliveries given by Nicolson (1942) and Lawrence (1949). In each case locking was by the forecoming head of the second twin below the aftercoming head of the first twin. High tone of the uterus with strong contractions pushing the second head down into the pelvis before delivery of the first twin was complete, was the only constant aetiological factor. Most of these babies were of moderate size for this country, and in no case was there evidence that the twins were not alive at the beginning of the second stage of labour, though by the time the mother was admitted maceration was usually advanced.

Delivery was completed by a destructive operation in all but one case, generally perforation and disimpaction of the second head and extraction of the first twin. In the one case in which the second twin was alive, the body of the breech was removed by decapitation, the head displaced and a live baby delivered by forceps. Considerable necrosis of the vagina resulted from the prolonged pressure, though in only one case did a vesico-vaginal fistula develop.

(2) *Head Born Before Admission, Shoulders Impacted*

These 7 cases occurred in women delivering at home without skilled assistance, and in 4 patients delivery was completed by traction under anaesthesia. Cleidotomy was required twice, and the remaining patient died undelivered soon after admission.

The following two cases illustrate this condition:

Case 1. Para-3, 7 days in labour, head born 15 hours. She was too exhausted to push out the body and a considerable amount of traction failed to deliver the foetus. On admission a cleidotomy was performed and a putrefying foetus weighing 6 pounds 11 ounces was extracted. She remained moribund and semiconscious for several days. The vagina sloughed resulting in huge vesico-vaginal and recto-vaginal fistulae, bilateral foot-drop developed and large pressure sores over the sacrum. She ran a swinging temperature, the bed sores became infected and she died on the 27th post-partum day.

Case 2. Para-2. The head was born 5 hours. She then walked several miles to the road and travelled 20 miles by lorry to hospital, taking a further 4 hours. The foetus was extracted easily under anaesthesia, and weighed 6 pounds 5 ounces. The vagina sloughed, left foot-drop developed but she eventually recovered.

(3) *Retained Aftercoming Head*

In the 6 patients in this group the aftercoming head had been retained from 6 to 17 hours on admission to hospital. Delay was at the brim rather than at the outlet, and due to extended arms, disproportion, posterior position of the occiput or in one case to hydrocephalus. Craniotomy was required for 3 of the deliveries. In 3 out of the 6 patients, the uterus was ruptured, there being 1 anterior tear and 2 posterior tears, and both the last two patients died. It is possible that attempts at delivery at home were responsible for these tears, and that they had been produced after the foetal body was born, as labour had been rapid and normal up to the birth of the breech.

IV. Face and Brow Presentation

Impaction of a face or brow presentation at the pelvic brim was found in 15 patients; in 8 cases it was a brow presentation and in 7 a face presentation, 5 of these mento-posterior. In 2 cases the baby was a second twin, but apart from these they were fairly large babies, all over 6½ pounds. Two women were admitted unconscious with eclampsia, obstructed labour with an impacted face presentation being an incidental finding.

Further extension and rotation made it possible to deliver 2 patients with forceps; Caesarean section was performed 5 times when the foetus was alive, and the remainder were delivered by craniotomy, or in the 5 cases of ruptured uterus, by laparotomy. There were no maternal deaths.

V. Compound Presentations

Labour was obstructed in 4 multigravidae, by 2 or more parts of the foetus entering the pelvic brim together. All these patients were admitted late in the second stage of labour, with the foetus already dead and in 2 cases the uterus ruptured. Delivery was accomplished by craniotomy and extraction or the foetus removed at laparotomy.

VI. Vaginal and Cervical Stenosis

Stenosis of the vagina is a fairly common finding among Nigerian women. Though many result from injuries of childbirth such as scarring

associated with vesico-vaginal and recto-vaginal fistulae, a certain number are congenital in origin or are caused by insertion into the vagina of some corrosive native medicine. This form of treatment is used especially at the time of the menopause to restore menstrual function, but is also used for threatened abortion and sterility. Stenosis was attributed to this cause in 2 cases. In the third case scarring from a large untreated vesico-vaginal fistula was so extreme that it was impossible to extract a macerated foetus weighing 3 pounds 10 ounces vaginally, even after embryotomy. Though female circumcision is a common practice in some districts, scarring was never sufficient to cause obstruction.

VII. Constriction Ring Dystocia

In 2 patients a constriction ring at the junction of the upper and lower segment prevented delivery of the second twin. The first babies had been delivered quickly and normally, with no intra-uterine manipulations and no drugs administered. Both cases are described.

Case 1. Para-6, 5 living, 4th pregnancy ended by Caesarean section for placenta praevia. The first twin weighing 4 pounds 12 ounces, was delivered normally after a labour lasting 30 hours. The second head presented and after 15 minutes a low rupture of the membranes was performed. In spite of good contraction, labour did not progress, and an hour later a vaginal examination revealed a constriction ring below the head at the junction of the upper and lower segments with the cervix hanging loosely below it. On touch the ring closed down from 3 fingers to barely 1, and in 3½ hours despite sedation the findings were identical. With morphia she slept intermittently until morning, but again the ring closed immediately it was touched. Deep anaesthesia, amyl nitrite and a caudal block all failed to relax the ring, and on the following day there was no change in her condition. A classical Caesarean section was performed and a live baby weighing 5 pounds 7 ounces was delivered just over 48 hours after the birth of the first twin. The puerperium was complicated by rupture of the uterine and abdominal wounds and a pelvic abscess, but she and the babies were eventually discharged well.

Case 2. Para-3, 1 alive. This patient was admitted having delivered a stillborn first twin at home 19 hours previously, after 1½ hours in labour. The foetal heart was still present, and on vaginal examination the head was felt above a vigorously contracting ring with a hand prolapsed through the ring. The cervix was hanging loosely, but the arm was cyanosed and oedematous from compression. Remembering our experience with Case 1, a Caesarean section was performed at once, without attempting relaxation, the baby being extracted with some difficulty through a transverse incision above the ring. The baby weighed 4 pounds 13 ounces and did well.

In neither case was the ring suspected until discovered at vaginal examination, nor was a history of colicky uterine pain elicited, perhaps due to inadequate questioning. The position of the rings, completely below the foetus and not round the neck is unusual (Louw, 1948), but it is probably explained by the presence of twins, the ring closing down below the intact sac of membranes, and is analogous to the hour-glass contraction of the uterus seen in the third stage of labour. The main criticism of treatment is the extreme conservatism exhibited in the first case.

VIII. Foetal Abnormalities

Malformations of the foetus causing obstruction occurred 12 times, and are briefly summarized though some cases are included under other headings.

Hydrocephalus, 7 cases, 2 maternal deaths.
Anencephalus, shoulder dystocia, 1 case.
Achondroplasia, 1 case.
Dicephalic monsters, 2 cases.
Meningocele, 1 case.

Two cases of rupture of the uterus occurred, one due to a hydrocephalic foetus, the other to an achondroplasic foetus with an exceptionally large head, and both these women survived. The maternal deaths were due to infection and occurred in each case within a couple of hours of delivery.

Delivery was by destructive operation in all but 2 cases. The dicephalic monsters presented the greatest problem. Both presented by the breech, and craniotomy of one head reduced the bulk sufficiently to allow vaginal delivery. One, weighing 4 pounds 11 ounces, was associated with a normal second twin, the other weighing 10 pounds was extracted with considerable difficulty.

Complications of Obstructed Labour

(1) *Maternal Deaths*

Booked primigravidae 3; emergency primigravidae 11; booked multigravidae 2; emergency multigravidae 28. Total 44.

With the exception of one death due to inhalation of vomit, three factors, in varying

degrees are responsible: shock, haemorrhage and infection, and it is often impossible to say which predominates. In addition the patient's resistance may be lowered by endemic local diseases such as malaria, intestinal parasites particularly *Entamoeba histolytica* and ankylostomiasis, and many are malnourished and anaemic.

Twenty-seven of the 44 maternal deaths were associated with rupture of the uterus, and all these women died on or before the 3rd post-partum day. If the patient dies undelivered or within a few hours of delivery, shock and blood loss predominate, while the longer she survives the more important becomes the role of infection. The clinical picture is often difficult to interpret as an overwhelming infection is characterized by rapid and progressive anaemia and circulatory collapse.

Six women died undelivered, 10 within 6 hours of delivery and a further 10 between 6 and 24 hours post-partum. Only one patient survived longer than 3 days. Pulmonary embolus is a condition we have never encountered among Nigerians.

(2) *Infection*

Using the old standard, 49·4 per cent of these patients showed a puerperal pyrexia. This figure included 34 women who died undelivered or too early to be assessed by these standards.

The majority of these infections and certainly all the fatal cases were primarily uterine, frequently with spread to the peritoneum and in severe cases an overwhelming bacteraemia presenting as circulatory collapse and progressive anaemia, and difficult to differentiate from internal haemorrhage. Infection develops and progresses in the tropics with a rapidity unknown in colder climates as is shown by the fact that 43 of the 44 maternal deaths occurred on or before the 3rd post-partum day. Bacteriological investigations were unfortunately not undertaken in all patients, but in those investigated *Escherichia coli* and aerobic streptococci predominated. Only 2 patients died of *Clostridium welchii* infection.

(3) *Urinary Complications*

In many women admitted in advanced labour the bladder was grossly distended and the passage of a catheter impossible until disimpaction or reduction in size of the foetal head. It was sometimes necessary to aspirate the bladder through a fine bore needle before the lower segment could be incised, and on several occasions the oedematous distended bladder was opened inadvertently, and repaired without ill effects. Haematuria was present in all cases of rupture of the uterus and in many of advanced obstruction, and cleared within 1 to 2 days of delivery. Temporary paralysis of the bladder was frequent in these cases and continuous drainage necessary for some days. Where there was definite sloughing of the vaginal wall, drainage was continued until it was obvious either that a fistula had developed or that the slough had separated and that the vagina and bladder were healing. Infection was seldom a serious problem.

A vesico-vaginal fistula developed in 21 cases, all emergencies, 10 patients being primigravidae and 11 multigravidae. Three women were delivered by Caesarean section with no additional trauma to the uterus, and in 2 cases a small slough separated and a temporary fistula healed spontaneously. All sizes of fistulae were seen, from a small mid-bladder defect easily repairable, to complete destruction of the entire vesico-vaginal septum from urethra to cervix, with extensive scarring and fixation to bone, and frequently associated with a recto-vaginal fistula. Of the 21 cases, 2 fistulae healed spontaneously, 10 were repaired, 1 patient died before repair was possible, and 9 patients remained untraced, but may have reported later under different names. In addition a long-standing fistula dating from a previous obstructed labour was found in 2 patients. Operative repair was never undertaken until 3 months post-partum.

(4) *Sciatic Nerve Paralysis*

Only 7 women are recorded as developing foot-drop, though mild cases may have been overlooked, and in some severely ill women dying within a few days of delivery, the paralysis may have been obscured by the patient's critical condition.

In 6 patients the foetal head presented, though in 2 of these the head was already born with the shoulders impacted. The breech presented in the 7th case, and was extracted with craniotomy of

the aftercoming head. All these women had been in the second stage of labour for many hours on admission, and it is suggested that the paralysis is in part due to stretching of the sciatic nerve from squatting for long periods while bearing down, as well as direct pressure from the impacted presenting part. Certainly a soft breech completely above the brim is unlikely to do much injury. Follow-up has been inadequate, but in all but the mildest cases recovery is incomplete.

(5) *Rupture of the Uterus*

Primigravidae 3 cases, deaths 3; multigravidae 65 cases, deaths 24. Total 68 cases, deaths 27 (40·3 per cent).

With one exception, these 68 cases of ruptured uterus were all spontaneous, either from overstretching of the lower segment or necrosis from pressure of the presenting part against the promontory or pubes, or a combination of the two. The remaining patient, a para-6, was admitted after 6 to 8 hours in the second stage with a high head and a doubtful foetal heart. As it was considered unjustifiable to perform a Caesarean section, forceps were applied tentatively before perforation of the head. With considerable traction the baby was delivered, but a large area of lower segment was avulsed, the tear extending into the peritoneal cavity. The baby sustained a large depressed fracture of the frontal bone from pressure against the sacral promontory, but was the only child in this series to survive.

Sixty-five patients were admitted with the uterus already ruptured, while 3 ruptured in the labour ward. The overall incidence of ruptured uterus in the hospital cannot be calculated from this series as many ruptures of doubtful origin or of Caesarean section scars are not included, only those definitely associated with obstructed labour, for which the incidence is 21 per cent.

Three of these patients were primigravidae, all admitted in prolonged labour lasting from 2 to 5 days, in poor condition, and all died soon after admission. The rupture was confirmed in 2 of these patients post mortem, while the third died during operation. The primiparous uterus responds to obstruction by hypotonia and diminishing activity (Jeffcoate, 1950) and pressure necrosis plays the major part in the causation of these tears. Extremes of parity are rare, rupture in the 2nd, 3rd and 4th pregnancy being the commonest.

If the foetus is extra-uterine the diagnosis is generally easy and can be made with certainty by abdominal palpation alone. The foetus is felt superficially and separate from the contracted uterus, and signs of shock and exsanguination confirm the diagnosis. In many cases the foetus is still either wholly or partially inside the uterus, either because the presenting part is wedged in the brim or is outside the vulva, or because of the site of rupture. With a posterior tear, occurring 23 times, it is seldom that the foetus can escape from the uterus. In such cases the diagnosis may be uncertain until extraction of the foetus permits adequate exploration of the uterus. The foetus is always dead, and except in one patient in whom the foetus was extruded through the tear complete in its sac, the membranes are ruptured.

Posterior tears were seen only when the head was impacted in the brim or with retention of the aftercoming head, and are largely due to pressure necrosis rather than overstretching, as is evident when attempting to repair the posterior tear, the sutures cutting out from the friable uterine wall. The distinction between complete and incomplete tears depends largely on the site and duration of the rupture. A lateral vertical tear between the leaves of the broad ligament may present with an enormous haematoma, the uterine artery may be torn and yet the peritoneum be intact especially if the foetal head is fixed in the brim, with the foetus still in the uterus. Contraction of the uterus may eventually expel the foetus which then acts as the agent converting the incomplete into the complete tear. The danger of not repairing a 5-inch tear of the uterus just because the peritoneum had been reflected by clot and is intact, is enormous, and the uterine scar, should the patient survive, will be totally unfit to withstand another pregnancy.

With little previous experience of this abnormality, a hysterectomy was performed in the first few cases, but it was rapidly appreciated that the quickest and least traumatic operation gave the best chance of survival. The majority of

tears are now repaired in 1 or 2 layers to control bleeding, and the tubes ligated. A few women with small anterior tears have not been sterilized, and one of these has been delivered twice since the rupture by Caesarean section. It is interesting that at operation the scar of the rupture could neither be seen nor felt. In the majority of cases, however, necrosis and muscle damage preclude all possibility of a sound scar capable of withstanding another labour. Occasionally the rupture is so extensive that repair is impracticable, or the tears may be multiple. It is often impossible to remove the foetus through a posterior tear, so that an anterior incision has to be made, making hysterectomy essential. Leaving the sutured uterus does not appear to increase the chances of infection and has the advantage, in this country, that the woman continues to menstruate.

Vaginal delivery should never be attempted on a patient with a definite rupture, and especially if part of the foetus has escaped through the tear. To minimize delay, all patients in whom a rupture is suspected are delivered in the theatre, the uterus explored post-partum and an immediate laparotomy performed should a tear be felt. Though some resuscitation is necessary, more is lost than gained by lengthy procedures, and we rarely delay longer than to obtain compatible blood, and run in the first pint quickly. Several of the patients in this series were operated upon when pulseless and with unrecordable blood pressure readings, yet they survived. Should the uterine artery be torn it will bleed at a more rapid rate than the blood transfusion running into the vein.

The 27 deaths all occurred within 3 days of delivery, and were due to varying combinations of the three main factors, shock, exsanguination and infection.

Comment

These problems are by no means confined to Nigeria; similar cases must occur in any underdeveloped country where the medical services are inadequate for both the size of the country and the population, and where the patients themselves frequently fail to avail themselves of such facilities as exist. A smaller but comparable series of cases, published from a hospital in West Bengal (Ghosal, 1953) shows a diagnostic pattern identical with that seen here. As here, obstruction due to fibroids or ovarian cysts did not occur in spite of the frequency of these tumours in young women; brim disproportion often associated with posterior position of the occiput was the commonest cause, and following this impacted transverse lie. Sepsis was universal, 2 patients developed tetanus, the majority of patients lost sufficient blood to constitute a post-partum haemorrhage, and their maternal deaths were due to sepsis or rupture of the uterus.

The incidence of gross abnormalities, such as locked twins, is exaggerated owing to the need to bring these abnormal cases to hospital for delivery. Multiple pregnancy is, however, more frequent in Nigeria, and in unselected booked patients twins occurs once in 24 deliveries.

The choice of treatment was governed to a large extent by local conditions and customs. Abdominal delivery was only contemplated if there was a possibility of a live child, as few women would deliver a second time in hospital after Caesarean section and a stillbirth. Destructive operations are preferred to Caesarean section if the foetus is dead, and are generally much quicker and easier. Similarly repair of the uterus is preferred to hysterectomy as a woman who ceases to menstruate, and is, therefore, sterile at an early age, may be divorced and returned to her parents in disgrace.

It is realized that a comprehensive study of obstructed labour cannot be made without accurate pelvic assessment, but X-ray films were scarce and the apparatus unreliable. The incidence of contracted pelvis is clinically high, the promontory being reached in the majority of women. Kaltreider (1954) of Baltimore found in a mass pelvimetry series that in 10 per cent of Negroes the pelvis was contracted, and all these patients would be of West African origin and many from this area. Sibthorpe and Allbrook (1958) in East Africa, working among Bantus, described a pelvis of similar characteristics.

All the maternal deaths and most of the stillbirths were preventable, though not with local conditions as they are now. Even with such inadequate antenatal care as was then possible, there was a dramatic improvement in the results

between booked and emergency patients. It is not, however, just a question of improving antenatal facilities. Education of the patient, better social conditions, transport, and improved diagnostic skill and treatment are all important.

Summary

Three hundred and twenty women in whom labour was obstructed were delivered in a hospital in Southern Nigeria, during the 4 years, 1953 to 1957. The ratio of primiparae to multiparae was identical with that of all hospital admissions, 30 per cent. Cephalo-pelvic disproportion at the brim, generally associated with a posterior position of the occiput accounted for 67 per cent of these cases, with impacted transverse lie next in frequency. Except for the incidence of rupture of the uterus, and transverse lie, the degree of parity is of little significance. The major complications, rupture of the uterus, vesico-vaginal fistula and sciatic paralysis are discussed briefly.

Though from clinical examination a fairly accurate assessment of pelvic size and shape can be made, no detailed radiography was possible owing to limited facilities. The average Nigerian pelvis shows great similarity to the Bantu pelvis described by observers in East Africa.

The great majority of these conditions and most of the 44 maternal deaths are preventable with better antenatal and hospital treatment, with improved social conditions and education of the patient.

I wish to express my thanks to my colleagues, Dr. J. B. Lawson and Dr. Kathleen Drury for permission to include some of their cases in this series.

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PREGNANCY FOLLOWING RADICAL VULVECTOMY FOR CARCINOMA OF THE VULVA

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PREGNANCY following a radical operation for carcinoma of the vulva is rare for two reasons. Firstly, this disease usually occurs in the older age groups, in fact post-menopausal women predominate. Secondly, as a result of the operation there is frequently such contraction of the vaginal orifice that coitus is impossible.

In regard to age incidence the Registrar General's Office has kindly supplied us with figures which have not yet been published. Care has had to be taken between the Registrar General and ourselves on the definition of the word "Vulva". Gynaecologists use the word as a collective noun for all the superficial structures in the area bounded by the mons veneris anteriorly, the perineum posteriorly and the genito-crural folds on each side laterally. The figures supplied by the Registrar General are for Cancer Registrations in the years 1952, 1954 and 1955 (those for 1953 are not yet adequately checked) and are the total number of cases reported to him affecting the vulva, the labia majora and the clitoris—each of which he enumerates separately. Out of a total of 920 cases 22 or 2·3 per cent are under the age of 40 and 56 or 6·1 per cent under the age of 45. Of the patients recorded in this communication the youngest is 19 and the oldest 39.

A comment on post-operative contraction of the vaginal orifice, its effect and its prophylaxis is recorded later in this communication.

The literature on this subject is very scanty. Heimann in 1931 described a patient who had vaginal deliveries 6 and 9 years after a radical vulvectomy. Way (1951) briefly reported Case No. 2 of this series in his book and also therein referred to a personal communication he had received from Haultain describing a patient who had a Caesarean section following a radical vulvectomy for carcinoma of the vulva. Collins *et al.* (1951) mention a case who also required Caesarean section for her delivery. Rubin and Lewis (1953) have reported a normal delivery following this operation.

Recently Collins and his colleagues (1958) have described a series of 41 cases of non-malignant conditions of the vulva for which they carried out an extensive excision of the vulva without lymphadenectomy. Eleven of these were under the age of 40. They comment that of the 41 patients: "Twenty of the patients were still young enough to be interested in sexual intercourse. Of these, intercourse was normal and orgasm attained in 17. Three others reported that intercourse was engaged in but there was no orgasm. Two of the 3, however, did not have orgasm on intercourse prior to operation. Three of the patients have become pregnant since operation. One has become pregnant twice since operation and each time was delivered normally *per vaginam* without complication. Each child weighed over 7 pounds (3,175 g.). Another was

delivered of a term 8 pounds baby (3,680 g.) normally *per vaginam* without any complication. A third patient is now [i.e., at the time of writing this paper] 26-weeks pregnant and a normal delivery is contemplated." Normal delivery did in fact take place (Collins, 1959).

Case Histories

The case histories are presented in ascending order of age at the time of operation.

Case 1 (O.L.)

Mrs. M.K., *née* Brown, attended the Gynaecological Out-Patient Clinic for the first time on the 12th January, 1950. She complained of soreness of the vulva of 6-weeks duration and was sent up by a doctor because he thought she had a small wart.

On examination, this unmarried girl, aged 19, was fit and well, and pelvic examination revealed no abnormality except for a small "warty" lesion about half an inch (13 mm.) in length and quarter of an inch (6 mm.) across on the left labium majus.

This girl admitted pre-marital intercourse about two months before she came to the clinic and, therefore, the Wassermann and gonococcal fixation tests were carried out and were negative.

In the meantime arrangements were made for her to be admitted for biopsy.

On the 18th January, 1950, under a general anaesthetic, the situation was reviewed and it seemed reasonable to carry out local excision of the tumour rather than take pieces from it, and this was done. Dr. Barrett reported a well-differentiated squamous carcinoma.

Because of the age of the patient and the very small lesion, which had been completely excised, radical vulvectomy was not considered to be a procedure to be recommended without prior consultation with someone of wider experience. Stanley Way was consulted and strongly advised radical surgery and, again, because of his wide experience of the operation, he was asked if he would care to come to Cambridge and do the operation as a demonstration case. This he did on the 18th February, 1950.

The operation notes record that the area on the left labium majus had healed by first intention. First, dissection of lymph nodes was carried out on both sides as far as the bifurcation of the common iliac veins. Soft enlarged nodes were encountered on both sides but, when examined microscopically, were found to be free from growth. The vulva was then excised with diathermy. A self-retaining catheter was inserted and the patient was transfused with one pint of blood on the table. The wound was dressed with topical thrombin and tulle gras.

Post-operative progress was satisfactory, the wound gradually healing with the assistance of occasional exposure to ultra-violet light but there was a good deal of granulation tissue surrounding the vaginal orifice.

Bearing in mind the possibility of contraction of the introitus which might lead to difficulty if the patient married, digital dilatation was performed. The patient was instructed in the use of glass dilators and a plastic obturator was prepared which she was able to insert herself.

She was seen at intervals during the few months after her discharge and gradually the operation scars became keloid to quite a marked extent but at no time was there any sign of recurrence. She was instructed to continue with the vaginal dilator until she decided about getting married.

When seen on the 16th January, 1951, some contraction of the orifice had occurred and she was unable to introduce the obturator so she had a further course of treatment with dilators. Eventually she married and when seen in February, 1952, was already 16-weeks pregnant.

There was no dyspareunia and no evidence of recurrence. It was decided that Caesarean section would be the best method of delivery and this was successfully carried out in June, 1952. (Male child, weight 4 pounds 4 ounces (1,930 g.).)

She subsequently attended at intervals and remained well. In 1954 she was found to be pregnant for the second time. Caesarean section with sterilization was carried out in August, 1954, resulting in the delivery of a male child weighing 6 pounds 7 ounces (2,920 g.). In November, 1954, the abdominal scar also showed keloid changes; otherwise she was quite well.

She was seen once a year in 1955 and 1956; and in June, 1956, she noticed a small lump in the right groin but this disappeared when she lay down and it appeared to be a small hernia in the right femoral region. This remained the same and when she was last examined on the 18th March, 1958, she was well and free from recurrence. In February, 1959, she reported by letter that she was well and able to lead a normal married life.

Case 2 (S.W.)

The patient Mrs. L.R. had a radical vulvectomy performed for two separate primary carcinomas of the vulva (one on the clitoris and the other at the upper end of the right labium majus) in October, 1944. She was then 28 years of age, married and nulliparous.

Histologically both tumours were well-differentiated squamous carcinomas. The lymph nodes were not involved. The patient made a good recovery from the operation but severe stenosis of the vaginal introitus occurred.

In March, 1946, coitus was said to be almost impossible and enlargement of the introitus was requested. In May, 1946, however, before she could be admitted to hospital for this operation she reported a period of 2-months amenorrhoea and clinical examination showed that she was pregnant.

It is interesting to note that before operation this patient showed no clinical signs of leukoplakia nor did histology of the removed specimen show any microscopic evidence of accompanying leukoplakia. When she was 4-months pregnant she developed leukoplakia of the perineum, anus and post-anal skin which became worse

as the pregnancy developed but, apart from this, the pregnancy was uneventful.

The contracture of the introitus with rigid scar tissue was such as to preclude any possibility of vaginal delivery without a most extensive episiotomy which was considered unwise. On 20th December, 1946, she was delivered at term of a living female child weighing 7 pounds (3,175 g.) by lower segment Caesarean section. Both mother and child did well and the puerperium was uneventful.

In August, 1947, nearly 3 years after the original operation she again complained that intercourse was unsatisfactory but refused any operative interference to enlarge the introitus. In September, 1949, she became pregnant again. A mild toxaemia of pregnancy necessitated her admission to hospital in March, 1950, and, on the 3rd April, 1950, she was again delivered at term of a living male child weighing 6 pounds 10 ounces (3,910 g.) by lower segment Caesarean section.

The patient remained well and both children flourished, but from time to time she continued to be troubled by the perineal and anal leukoplakia.

In 1958, a warty-like hyperkeratotic lesion appeared in the middle of the perineum and in May, 1958, as a result of increasing irritation, the perineal skin with the area of hyperkeratosis was excised. Histologically this showed an early differentiated squamous cell carcinoma. Since this time the patient has remained symptom-free and, when last seen in January, 1959, she was very well and both children, one aged 12 and the other almost 9, are in excellent health.

Case 3 (A.B.)

Mrs. I.D., aged 30, nulliparous, was seen in May, 1953. She complained that she had had an increasing number of warts on the vulva for 9 years. They had caused soreness for 6 months and in the last 2 months there had been pain and intermenstrual bleeding.

Examination showed the right labium majus replaced by a papillomatous mass of confluent warts (condylomata acuminata). The anterior half of the left labium majus showed a similar mass of warts and its posterior half a tender sloughing ulcer. There were massive peri-anal confluent warts (Fig. 1). Biopsy from the ulcer showed a squamous carcinoma.

On the 17th June, 1953, a radical vulvectomy was performed and the peri-anal condylomata treated by electro-coagulation. Dissection of the glands was confined to the superficial and deep femoral groups on both sides. The left external iliac glands were explored suprapubically but as they were not enlarged they were not removed. Sections of the femoral glands showed no evidence of metastases. The peritoneum was inadvertently opened and bilateral chronic salpingitis was noted with several uterine fibroids, one the size of an orange. On 15th July, 1953, residual anal warts were treated by further electro-coagulation.

In March, 1956, she reported herself to be pregnant. The uterus was found to be larger in size than would conform with the period of amenorrhoea and small fibroids could be felt. The operation area was healthy. At her 34th week protein was present in a catheter specimen of urine and her blood pressure was 150/80. She was admitted for observation. During the three and a half weeks that she was observed her blood pressure ranged at about 130/90 and there was ½ gram of protein in her urine throughout.

Caesarean section was performed on 26th September, 1956, and a male child of 5 pounds 8 ounces (2,495 g.) was delivered. At operation two soft red fleshy tumours and several seedlings were noted on the uterus. Biopsies were taken from these. Sections showed the tumours to be fibroids and there was no evidence of malignancy.

This patient has not attended well for follow-up visits. Two years after the operation the area was well healed and free from recurrence (Fig. 2). In April, 1959, she reported herself as well and free from recurrence but preferred not to be examined on that occasion as she was menstruating.

Case 4 (S.W.)

Mrs. C.C., aged 30, was attending the Venereal Clinic of the Newcastle General Hospital for treatment of syphilis. She had had 2 female children both normal deliveries, one in 1943 and one in 1945 and in 1950 she had been delivered of a stillborn syphilitic child which was a month premature. Her husband, also a syphilitic, resolutely refused to have any treatment. Mrs. C.C. only had what was, probably, an incomplete course of anti-syphilitic treatment.

During the course of her treatment in February, 1951, she was referred to Miss C. A. Grey at Bensham General Hospital, Gateshead, with a small hypertrophic tumour ¾ inch (2 cm.) in diameter on the right labium majus. This was widely excised and proved to be a fairly well differentiated squamous carcinoma. Ten days later a radical vulvectomy was performed. The lymph nodes were not involved. The wound healed rapidly and the vaginal introitus was very capacious, four fingers being inserted with ease.

She remained well with no evidence of recurrence and in September, 1952, at a follow-up visit she was found to be 3-months pregnant. She was referred back to Miss Grey at the Maternity Department, Queen Elizabeth Hospital, Gateshead, with a suggestion that since the introitus was so capacious a normal delivery seemed very possible. In January, 1953, she developed a mild toxaemia of pregnancy which necessitated her admission to hospital and, whilst undergoing treatment for toxaemia in February, 1953, she had a spontaneous normal delivery of a male child of 7 pounds 8 ounces (3,400 g.) without any assistance. There was no evidence of recurrence of the carcinoma of the vulva at this time, 2 years after operation.

This patient has been a very poor attender at follow-up clinic but was last seen in the spring of 1958, 7 years after operation and 5 years after her first post-operative delivery when she was again found to be pregnant and had a normal delivery of another female child of 6 pounds 8 ounces (2,950 g.) in the summer of 1958. Since that time she has refused to attend any postnatal or follow-up clinic.

Case 5 (A.A.G.)

Mrs. M.G., aged 31, married, with 3 children was seen in Out-Patients on 26th January, 1953. She complained that for the past 2 weeks she had noticed a painful area on the right side of the vulva which was now ulcerated. Examination showed a shallow ulcer ½ inch (13 mm.) in diameter in the groove between the labium majus and labium minus of the right side. No enlarged glands were found.

A Gonococcal Complement Fixation Test and a Kahn test both proved negative. On the 23rd February, 1953, the ulcer was excised and sent for examination. Sections showed hypertrophic leukoplakia with some areas of epithelioma.

There was delay due to the difficulty in persuading the patient to return to hospital and in making touch with her husband who was in Port Said with his ship. Eventually on 31st March, 1953, a radical vulvectomy was performed with excision of the superficial and deep inguinal glands with those in the femoral triangles. The lower part of the cut edge of the posterior vaginal wall was dissected free and stitched to the perineal skin, otherwise the wound was left to granulate. She had a haemorrhage from the symphyseal area on the second day which required suture. Apart from this convalescence was uneventful. The wound healed well and she was discharged from hospital on 11th June, 1953. Further sections confirmed the presence of epithelioma at the original site but no malignant disease could be found in any of the excised glands.

A month later she was seen in Out-Patients and the wounds were quite healthy. She had no dyspareunia.

Four months later still, i.e., 9th November, 1953, she reported again when she proved to be very well and was found to be 14-weeks pregnant. She was very well during the pregnancy except for a mild transient proteinuria at approximately the 36th week. The perineal portion of the scar, which had never been very fibrous, had softened completely and on 13th April, 1954, she had a spontaneous normal delivery after a small right posterolateral episiotomy. Labour lasted 11 hours and the female child weighed 8 pounds 2 ounces (3,685 g.). The puerperium and lactation were normal. Numerous sections of the placenta were examined and no evidence of metastasis was found.

The patient attended the follow-up clinic regularly and on 12th March, 1956, was again found to be in good health and pregnant.

She was again delivered normally on 24th July, 1956, of a female child weighing 7 pounds (3,175 g.), this time without an episiotomy. She was sterilized 2 days after delivery by tubal division and ligation.

She has attended the follow-up clinic regularly since this last confinement and was seen on 25th September, 1958. She reported herself as very fit and reaffirmed that there had been no diminution in libido or orgasm caused by the operation of 1953. On examination the vulval orifice gapes somewhat and there is some descent of the vaginal walls on straining (Figs. 3 and 4). The uterus and appendages are quite normal in size, position and mobility.

Case 6 (A.C.H.B.)

Mrs. O.S., aged 32, nulliparous but married for 2 years, was first seen in December, 1948, complaining of irritation of the vulva for 3 years, a "lump", and pain in the groins for the previous month. On examination the inner aspects of the labia minora were oedematous, and the clitoris was replaced by a fungating polypoidal mass ½ inch long (13 mm.). (Fig. 5.) There were enlarged and tender glands in the groins.

On the 16th December, 1948, the vulva was excised by Mr. G. Wynn-Williams and sections showed a well-differentiated squamous cell carcinoma.

On the 30th December, 1948, bilateral inguinal lymphadenectomy was carried out. The glands were found to be free from growth. Convalescence was uneventful, and she was discharged home 5 weeks from the date of the vulvectomy.

Routine follow-up has been carried out, without any sign of recurrence, to the present time.

In January, 1950, she became pregnant and booked at Queen Charlotte's Hospital. Her antenatal care and delivery were carried out by her own doctor. The estimated date of delivery was 22nd October, 1950, but she went into premature labour at home, and was delivered spontaneously of a male child weighing 4 pounds 7 ounces (2,015 g.) on the 23rd September (36 weeks). The duration of labour was not known but was estimated at about 4 hours. She was admitted as an emergency to Queen Charlotte's Maternity Hospital with a retained placenta. The duration of the third stage was 1½ hours. Her general condition was good, and the placenta was delivered by Credé's expression. The perineum was noted to be intact without any tear, although no episiotomy had been made. The puerperium was uneventful and the baby was healthy and fully breast fed.

Six months later she was fit but advised to wear an elastic stocking for varicose veins of the left leg.

On the 24th June, 1952, she complained of deep dyspareunia, and was found to have a left ovarian cyst. At operation on 28th August, 1952, a simple unilocular left ovarian cyst 2·4 inches (6 cm.) in diameter was removed; there was no sign of recurrence of the carcinoma of the vulva. The pathological report showed that the cyst was a simple one, and the cyst wall, which was composed of compressed ovarian tissue, had no epithelial lining.

In 1955 Mrs. O.S. attended Westminster Hospital for ligation of her varicose veins. She was last examined on 17th June, 1958, when she had no complaints. There was no evidence of recurrence locally or in the groins, and the pelvic findings were normal,

Case 7 (F.R.S.)

Mrs. N.M., aged 32, married, with one child aged 6 years, was seen in the Out-Patients on 9th February, 1953. She complained of vulval ulceration since November, 1952. Examination showed an ulcerated warty growth of her right labium minus close to the clitoris. There were atrophic vulval changes. There was no obvious inguinal lymphadenopathy. She had a past history of ulcerative colitis—subject to frequent exacerbations—but quiescent at the moment.

FIG. 2
Mrs. I.D. Two years after operation.

FIG. 1
Mrs. I.D. Before operation.

FIG. 3
Mrs. M.G. Five years after operation.

FIG. 4
Mrs. M.G. Five years after operation.

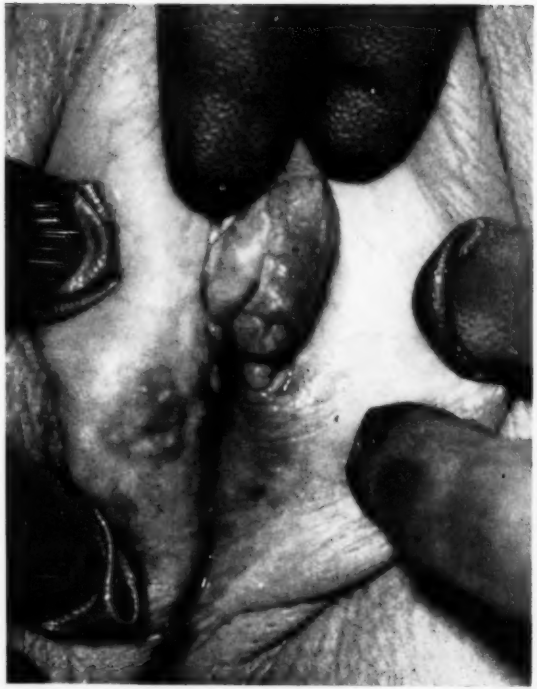

FIG. 5
Mrs. O.S. Before operation.

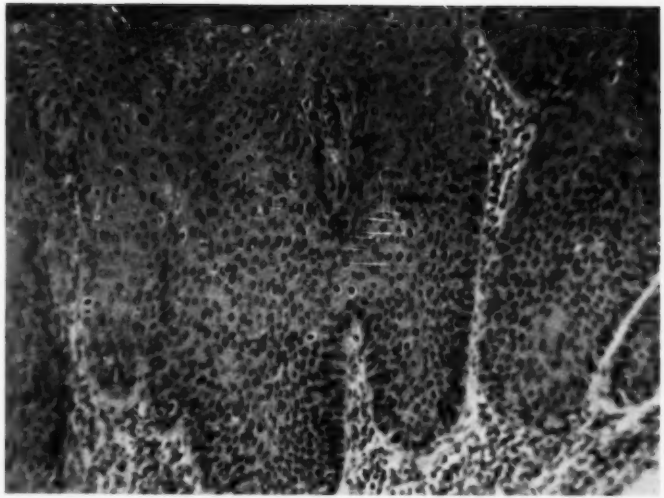

FIG. 7
Part of lesion of Case 5, showing intra-epidermal carcinoma. H. and E. × 60.

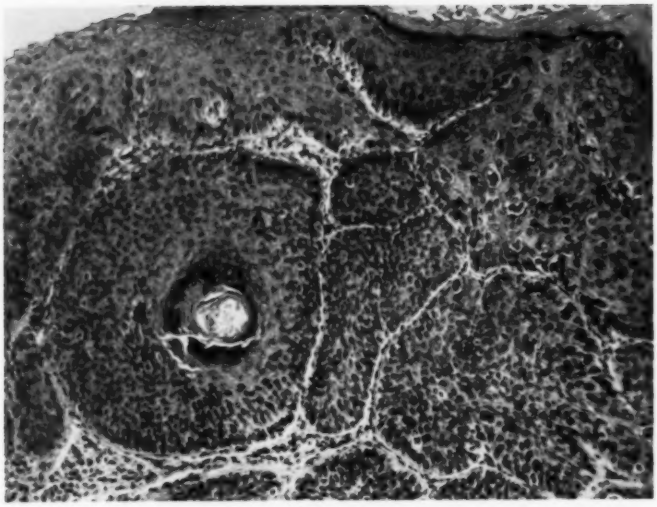

FIG. 8

Another part of lesion of Case 5, showing epidermal carcinoma and intra-epidermal carcinoma. H. and E. ×60.

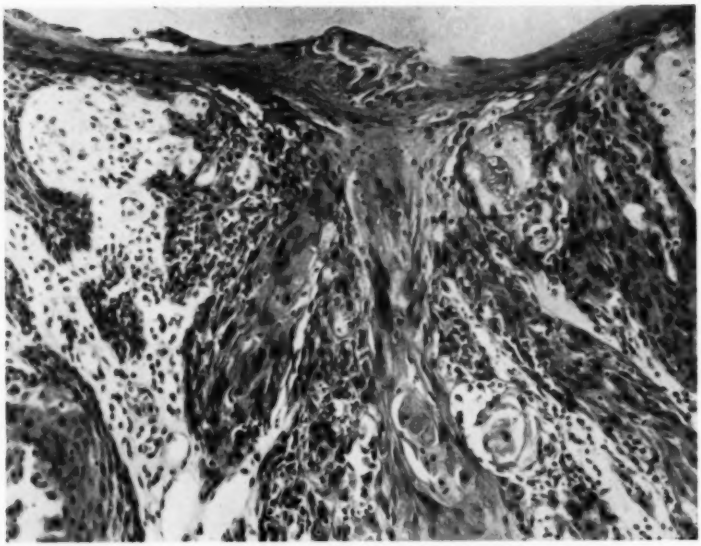

FIG. 9

General histological appearance of most of the cases. H. and E. ×60.

On 16th February, 1953, she was admitted to hospital. A Gonococcal Complement Fixation test and a Kahn test had both proved negative. On the 18th February, 1953, a radical vulvectomy was performed with excision of the superficial and deep inguinal glands with those in the femoral triangles. Convalescence was delayed slightly by the development of a haematoma in the left groin, but she finally made a satisfactory recovery and was discharged from hospital on 24th March, 1953. The pathological report was as follows: "On the right labium minus and involving the commissure there is a raised firm growth 1 inch × ½ inch (25 × 15 mm). The growth is a squamous carcinoma showing marked keratinization and prickle formation. No evidence of malignancy could be found in any of the excised glands."

One month later she was seen in the Out-Patients. The wounds were healthy, but there was a fibrous ring around the introitus. She felt well. She attended the Out-Patients Department at 2-monthly intervals during 1953 and at 6-monthly intervals afterwards. There was no evidence of any recurrence of her growth, but early in her post-operative course she developed prolapse of her urethra and anterior vaginal wall.

On September 16th, 1955, she presented with a history of 8-weeks amenorrhoea. Examination showed her to be pregnant. Her pregnancy progressed satisfactorily until the later weeks when she developed stress incontinence of urine.

On 20th April, 1956, she had a spontaneous delivery following an episiotomy of a living female infant, weighing 7 pounds 6 ounces (3,345 g.). Her episiotomy did not heal satisfactorily and, on 10th May, 1956, an anterior colporrhaphy and posterior colpoperineorrhaphy with sub-urethral repair was performed. Her subsequent progress was uneventful.

She has attended the follow-up clinic regularly and has shown an excellent result to both operations. There has been no evidence of any recurrence of her growth. She has had no dyspareunia or diminution in libido as a result of the operations. However, when seen on 20th March, 1959, she complained of loss of libido and frequency of micturition in the mornings. There is no evidence of recurrence of the growth.

Case 8 (*C.M.G.*)

Miss D.F., aged 33, attended the Out-Patients Department for the first time on 14th November, 1950. She complained of a soreness of the left side of the vulva which had been present for the last 2 weeks. Examination showed a proliferative carcinoma situated in the region of the clitoris and extending down both labia minora but more so on the left. The tumour was hard, tender and irregular in outline and bled easily on touching. The urethra was not involved. The regional lymph nodes were not palpably enlarged.

Wassermann and Kahn test were both negative. She was admitted to hospital on the 23rd November, 1950, and a biopsy from the tumour performed on the 25th November. This showed a well-differentiated squamous-celled carcinoma.

On 28th November, 1950, under general anaesthesia a radical vulvectomy and bilateral ilio-inguinal lymph-adenectomy was performed. Both inguinal ligaments were divided to enable the full dissection of the lymph nodes to be made. Apart from stitching the lower edge of the vaginal skin to the skin above the anus, no attempt was made at wound closure, the raw area being packed with tulle gras.

Her post-operative recovery was uneventful apart from an attack of influenza 3 weeks after the operation. She was discharged on the 30th January, 1951. Further pathological examination of the specimen confirmed a heavily keratinized squamous-celled carcinoma of the vulva and 7 nodes from the left and 5 from the right side showed only chronic inflammatory change but no metastatic deposits.

She was seen in Out-Patients on the 7th March, 1951, when she was found to be very well but considerable scarring around the introitus was noted. This did not respond to dilators and she was re-admitted in May, 1951, for a plastic enlargement of the vaginal introitus.

When seen in June, 1951, she was found to have a good result from this operation, the vaginal introitus being quite adequate.

She defaulted from follow-up and was next heard of when a letter was received from the Central Middlesex Hospital saying she had got married in 1952 and had been delivered by Caesarean section on the 16th July, 1953, of a male child of 7 pounds 6 ounces (3,345 g.). There was noted to be no evidence of recurrence in the vulval region or glands at that time and the patient herself was very well. There was a good deal of scarring around the introitus which necessitated the Caesarean section.

She was seen in the follow-up clinic in September, 1955, and in June, 1957, when there was noted to be no sign of recurrence.

Case 9 (*S.W.*)

Mrs. L.S., aged 39, nulliparous, was operated on in early February, 1949, for a well-differentiated squamous carcinoma of the vulva situated on the left side of the vulva just below the clitoris, ¾ inch (2 cm.) in diameter. The lymph nodes were not involved. A vaginal obturator made of stent was inserted during the healing period and the introitus at the completion of healing admitted three fingers.

In May, 1950, she reported a period of 7-months amenorrhoea. There were no breast changes but the uterus was soft and enlarged and had the consistency of an early pregnancy. Three days after this examination she had a complete abortion.

In November, 1951, she attended the clinic having had amenorrhoea since June of that year and was found to be 5-months pregnant. When 24-weeks pregnant her blood pressure suddenly rose from 120/80 to 160/95. No other signs of toxaemia were present. She continued at home under the care of her own doctor but in January, 1952, blood pressure rose to 180/120 accompanied by oedema of the legs and headaches but no proteinuria. She was at this time admitted to hospital. Three weeks later protein appeared in the urine. She remained in hospital for the

remainder of the pregnancy. Her hypertension subsided somewhat with rest in bed but the protein increased. On 8th February, 1952, the systolic blood pressure rose to 200. The foetal heart continued regular and was counted at hourly intervals. Suddenly on 12th February the foetal heart became very weak and immediately lower segment Caesarean section was performed under local anaesthesia and a male child of 4 pounds (1,815 g.) was delivered which unfortunately was stillborn. The patient made a good recovery from the operation but her blood pressure remained in the region of 180/100 for 7 months after which it returned almost to its normal level.

She has since remained well with no evidence of recurrence of carcinoma now, 10 years after operation, and at the age of 49 she is unlikely to become pregnant again.

The following case is included although it differs from the preceding cases in two important aspects. The operation was carried out during pregnancy and was not radical.

Case 10 (*C.K.V.*)

Mrs. K.M.P., aged 30, married but nulliparous, attended Out-Patients on 22nd June, 1954, complaining of a "small wart" on the vulva. She was found to have a small ulcer on the clitoris and to be about 20-weeks pregnant. On 29th June, 1954, the ulcer was excised and sections were reported as an early keratinizing squamous celled carcinoma.

She was re-admitted for more radical excision. On 27th August, 1954, a purely local excision was carried out by an inverted horse-shoe shaped incision (Fig. 6) embracing the clitoris and the labia minora and majora down to the muscle layer and stopping short of the perineum. A palpable superficial gland on the left side was removed for biopsy. Sections showed no evidence of metastasis.

At the time of this operation she was in the 22nd week of her first pregnancy. The pregnancy proceeded normally until the 34th week when she developed hypertension and proteinuria. She was admitted. Unfortunately she had an ante-partum haemorrhage at the 36–37th week and on 8th November, 1954, a Caesarean section was performed which might otherwise have been unnecessary. The child was a male of 5 pounds 1 ounce (2,295 g.) and was breast fed with a small complement.

FIG. 6
Mrs. K.M.P. Incision for operation.

She attended the follow-up clinic regularly and displayed no sign of recurrence. Seventeen months after her delivery she booked for her second pregnancy. This pregnancy remained normal until the 37th week when she again developed hypertension and a trace of protein. A planned Caesarean section with sterilization was carried out on 9th January, 1957. Another male child of 6 pounds 7 ounces (2,920 g.) was delivered and was also breast fed with a small complement.

The patient has been seen and examined in May, 1959. There is no evidence of recurrence, the vagina is normal and the introitus looks adequate. She now finds intercourse a little painful and only practises it occasionally.

HISTOLOGY (Magnus Haines)

Material was examined from 7 patients. Unfortunately no slides were any longer available from Cases 2, 4 and 9.

In 5 cases there was a similar pattern of mostly well-differentiated squamous cell carcinoma; invasion did not appear to go deeper than the superficial dermis. Histological changes of leukoplakia adjacent to the carcinoma were noted in 3 instances (Nos. 1, 8, 10). In 2 cases (Nos. 3, 5) there were points of special interest.

No. 3. This showed warty, papillomatous skin with, in numerous areas, irregular aberrant nuclear patterns, amounting in some places to intra-epidermal carcinoma. There was one patch of carcinomatous ulceration; although showing several small foci of keratinization, the squamous cell carcinoma was only moderately well differentiated.

No. 5. This was a localized disorder of the epidermis, predominantly leukoplakia but with foci of intra-epidermal carcinoma and a few areas of dermal invasion (Figs. 7 and 8).

None of the slides submitted showed lymph node metastasis but the material was incomplete.

Summary

In general the cases were of well-differentiated squamous cell carcinoma of limited extent and no evidence of spread beyond the dermis or in the lymph nodes was noted (Fig. 9).

In 2 cases there was intra-epidermal carcinoma but there is no evidence to show how long thi possibly antecedent lesion preceded carcinoma

Marital Relations after Operation

All 3 patients (Cases 4, 5 and 7) who were multiparous at the time of operation experienced no dyspareunia after it. Only in Case 5 can it be said that any deliberate step was taken in an attempt to avoid dyspareunia—dissecting free the posterior margin of the vagina and stitching it to the perineal skin edge.

Amongst the 6 nulliparous patients (Cases 1, 2, 3, 6, 8 and 9) definite steps were taken in 3 (Cases 1, 8 and 9) and none of these had dyspareunia. Cases 1 and 9 were treated by Stanley Way's method (see below) and in Case 8 contraction of the vaginal orifice was noted 6 months after operation and before marriage so surgical enlargement of the introitus was carried out and no dyspareunia was experienced at a later date. No special precaution was used in Cases 2, 3 and 6. Case 2 developed dyspareunia and became pregnant in spite of this; operation was refused. Case 3—no information is available. Case 6 had no dyspareunia.

Case 10 was pregnant at the time of her operation and the area excised stopped short of the perineum. She had no dyspareunia until 5 years later.

It appears from the above that patients who are parous show little tendency to excessive postoperative contraction of the introitus which may possibly be associated with a fairly early resumption of marital relations after return home.

There is not adequate information about libido and orgasm for a comment to be made. It will be noted, however, that in Case 5 both were retained.

Prevention of Stenosis of Introitus

When the vulval wound is left wide open and allowed to heal by granulation there is a very considerable risk of stenosis which may be sufficient to cause dyspareunia or even to prevent penetration altogether.

This can at least be minimized and in some cases entirely prevented by inserting a plastic obturator during the healing period.

The obturator is made of a solid bar of "stellon" 6 inches (15·3 cm.) in length and 2 inches (5·2 cm.) in diameter to the external end of which is attached by screws an x-shaped plate with holes at each of the four ends of the limbs. To these holes tapes are attached and these (two over the abdomen and two over the back) are fitted to a belt which is worn round the waist. In this way the obturator can be worn whilst the patient is ambulant. The instrument is based on the design of the Way Vaginal radium applicator (Way, 1948).

The optimum time for its insertion is when the granulating edges of skin approach to the vaginal mucosa by a distance of about 0·2 inches (0·5 cm.). It is usual to allow the patient to remove the obturator at night.

More recently the plastic flap closure method of Way has prevented stenosis occurring. By this method (Way, 1957) complete closure of the vulval area is achieved, unless the tumour is extremely large, by undercutting the skin and subcutaneous fat at the edge of the vulval excision and lifting it from the deep fascia for a distance of 2 inches (5·2 cm.). The legs are then removed from the lithotomy stirrups and held almost together. In this position complete closure of the vulval area can nearly always be achieved without any loss of the radical nature of the excision. The patient is nursed with her legs tied together. Following this technique stenosis is hardly ever encountered, indeed some degree of vaginal descent is more often the case.

This technique was not used in any case in this series.

Delivery (Table I)

Of the 9 patients who were not pregnant at the time of the vulvectomy, 4 (Nos. 4, 5, 6 and 7) had normal vaginal deliveries and 5 (Nos. 1, 2, 3, 8 and 9) were delivered by Caesarean section. The total number of cases is too small for any definite conclusions to be drawn as to the factors which determine the method of delivery. It is, however, of interest to note that the 3 women who were parous at the time of the operation all had normal vaginal deliveries and that the only one who was nulliparous and had a vaginal delivery had a premature labour resulting in the birth of a child weighing 4 pounds 7 ounces (2,015 g.).

Where delivery was by Caesarean section in only 2 (Nos. 2 and 8) was the indication the

TABLE I

Case No.	Age	Parity	Operation to Conception (months)	Weight of Child		Method of Delivery	Remarks
				Pounds	Ounces		
1	19	N(S)	22	4	4	Caesarean section	
			45	6	7	Caesarean section	
2	28	N	17	7	0	Caesarean section	Pregnant in spite of superficial dyspareunia
			59	6	10	Caesarean section	
3	30	N	30	5	8	Caesarean section	Toxaemia
4	30	M_2	16	7	8	Normal	
			84	6	8	Normal	
5	31	M_3	6	8	2	Normal	Small episiotomy
			26	7	0	Normal	
6	32	N	12	4	7	Normal	Premature
7	32	M_1	30	7	6	Normal	Episiotomy
8	33	N(S)	24	7	6	Caesarean section	
9	39	N	9	–	–	Abortion	
			33	4	0	Caesarean section	Toxaemia, fading foetal heart
10	30	N	Pregnant	5	1	Caesarean section	Toxaemia, accidental haemorrhage
			17	6	7	Caesarean section	

(S)=Single at time of operation.

extent of the scarring; in 2 other cases (Nos. 3 and 9) toxaemia was the chief indication.

In the patient (No. 10) whose vulvectomy was done during pregnancy a Caesarean section was undertaken on account of accidental haemorrhage.

It might be thought that the sooner after the operation conception occurred the greater the chance of softening of the scar. The small number of cases prevents any firm statement on this point. Cases 2 and 8 are the only two in whom scarring was the only indication for Caesarean section. Case 2 had much scarring immediately after the operation leading to dyspareunia. In Case 8 the operation–conception interval was 24 months. For the patients who had a normal vaginal delivery it was for Case 5—6 months, for Case 6—12 months, for Case 4—16 months but for Case 7 it was 30 months.

Cases 1, 2, 4, 5 and 10 each had 2 pregnancies after the vulvectomy and the method of delivery of the second child was, in each patient, the same as that of the first.

SURVIVAL

All 10 patients have, to date, survived the operation from 5 to over 14 years.

The after histories show no evidence that pregnancy subsequent to radical operation favours the development of a recurrence. The one patient who developed a recurrence (No. 2) did so 14 years after her original operation and 8 years after the delivery of her second child. It must, however, be stated that we have no records or knowledge of any patient, if such there be, who became pregnant after radical vulvectomy and rapidly developed a recurrence.

Four of our patients have had 6 normal vaginal deliveries between them. They have survived between 6 and 10 years so the dilatation, by childbirth, of the reconstituted vaginal orifice does not affect the prognosis.

Summary

(1) Case histories are presented of 10 patients who have had one or more viable pregnancies following vulvectomy for carcinoma of the vulva. In 9 the operation was radical and in one it was extensive and performed during pregnancy.

(2) The histology of the lesions is recorded. In all patients the lesion was found to be mainly superficial and in none was there any lymphatic spread.

(3) In only one patient was dyspareunia a troublesome post-operative symptom and she became pregnant twice in spite of this. Some steps to avoid post-operative dyspareunia are recorded.

(4) The method of delivery is recorded for all patients. In only 2 was the extent of scarring the indication for Caesarean section whilst 4 patients had 6 normal vaginal deliveries between them.

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THE GIANT CELLS OF THE PREGNANT HUMAN UTERUS

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FOR a number of years, in the course of studies on the development of the human placenta, we have made observations on the remarkable "giant cells" which are found in the decidua basalis and the adjacent myometrium during gestation. Attention was first directed to these cells by Kölliker (1871) in the first edition of his *Lehrbuch der Embryologie*. Kölliker called them *Riesenzellen* or *vielenkernigen Zellen* and he indicated that they are restricted to the decidua basalis. In the English literature they have usually been called giant cells, which term we will use in this contribution. Under such terms as "wandering cells", "migratory cells", "megalokaryocytes" and "diplokaryocytes", nucleated masses possessing certain similarities to the human giant cells have been described in the decidua of a number of mammals. Since Kölliker's first description most of those who have studied the giant cells have attributed a trophoblastic origin to them. There are, however, a number of accounts in the literature which suggest, or specifically state, that they are derived from maternal cells. In a recent contribution to the subject, for example, Park (1959) writes: "Almost certainly ... these giant cells are not always of trophoblastic origin. The only evidence suggesting that they are is morphological, but some of the tissue patterns can be interpreted morphologically in other equally reasonable or perhaps even more reasonable ways." After describing briefly elements in the decidua which he considers to be decidual cells in the course of becoming giant cells, Park adds: "By all ordinary standards of morphological identification these are multilobular and multinuclear decidual cells, not invasive trophoblast." He also considers that "uterine muscle, as well as decidua, can almost certainly produce giant cells". These statements have prompted us to record our own observations on the giant cells in human pregnancy. As will be seen our conclusions do not agree with those of Park.

MATERIAL AND METHODS

Our material includes over 100 *in situ* human implantation sites and placentae. It extends from the second week of development until full term. We also possess a number of post-partum specimens and non-pregnant uteri. It is not our intention in the present contribution to present full technical details and case histories of this material; such information will appear in a contribution we are preparing for publication elsewhere. It is, however, necessary to stress that many of the specimens are in excellent histological condition, having been obtained from hysterectomies and having been fixed under optimal conditions. Most of the material has been sectioned *in situ* in extensive series. Consequently it has been possible to study the full regional geography of the placenta at its successive developmental stages. The sections were

stained with a wide variety of histological methods including H. & E., trichrome, Azan, iron haematoxylin, PAS, Foot's reticular stain, Feulgen, chrome alum haematoxylin and a number of special histochemical techniques.

For present purposes we base our account essentially on selected specimens from appropriate periods of gestation. Consideration will be given to the origin, the general topography and the distribution of the giant cells. It is intended to present observations on their histochemistry in a later publication.

Terminology

Owing to the great confusion in the literature on the terms used to describe the different varieties of trophoblast which are found during human placental development it is necessary to present here, briefly, our own views on this terminology. The terminological problem is due in part to the difficulties inherent in any attempt at the description of the different histological appearances presented, at successive stages of development, by the differentiating syncytio- and cyto-trophoblast. The confusion is worse confounded, however, by dogmatic opinions expressed by certain investigators on the functions they believe to be subserved by the different trophoblastic derivatives at different times in their development.

All of the trophoblast is certainly derived from the zygote and, phylogenetically, it can be regarded as a precociously developed ectodermal derivative which has appeared in mammals in association with their adoption of viviparity. In the earlier stages of differentiation of the mammalian ovum the trophoblast is represented by the cells constituting the wall of the blastocyst. These cells are probably reinforced later by some contribution of elements from the superficial part of the inner cell mass. Certainly, however, the view of Gordon (1949) that cumulus cells, on the outside of the zona pellucida, contribute to the trophoblast will not bear any sort of analysis. In the stages just before attachment to the uterine mucosa we consider that the term *blastocystic trophoblast* is appropriate for the cells constituting the outer wall of the developing zygote. The observations of Hertig *et al.* (1954), on an unimplanted human blastocyst of about 108 hours ovulational age, indicate that the trophoblast at this stage consists entirely of separate cells and so, to this extent, can be regarded as undifferentiated. These investigators, however, distinguish between *polar* trophoblast cells, covering the inner cell mass, and *mural* trophoblast cells, which make up the remaining portion of the blastocyst wall. The mural cells are elongated and flattened and thus give the appearance of having been stretched by the accumulation of fluid. Cytoplasmic vacuoles in some of them are interpreted by Hertig and his collaborators as a possible source of the fluid in the blastocyst cavity. The polar trophoblast cells are more polygonal in shape; collectively these cells cover the superficial aspect of the embryonic inner cell mass.

In their paper on the early development of the macaque embryo, Heuser and Streeter (1941) described the early blastocyst in this primate as consisting of cavity-wall trophoblast cells (which, presumably, correspond to the mural trophoblasts of Hertig *et al.*) and polar trophoblast cells. At the embryonic pole of the 9-day macaque blastocyst, however, Heuser and Streeter considered that, in a relatively small region, there is a nodal centre of proliferation. They described the more superficial cells of this node as providing a special mechanism for invasion of the uterine epithelium. Indeed, these two investigators indicated that as early as the morula stage, and before the first appearance of the cleavage cavity, two types of cells can be distinguished. These are (1) the cells of the central mass, and (2) a single layer of cells which covers most, but not all, of the central mass. From this layer, in their opinion, the first (cavity-wall or mural) trophoblastic cells differentiate to form the special membrane through which fluid passes to reach the cleavage cavity. The central group of cells constitutes an undifferentiated inner cell mass from which, in subsequent development, formative cells and further (polar) trophoblastic cells will be segregated. Heuser and Streeter concluded that the trophoblastic cells thus tardily differentiated at the embryonic pole are specialized for purposes of attachment of the conceptus to the endometrium. While descriptively such an explanation may be acceptable it must be pointed

out that the development of the secondary placenta in the macaque demonstrates clearly that the ability to attach to the uterine mucosa is not restricted to polar trophoblast. This secondary placenta is constituted, on the embryonic side, by cells which have been mural, or cavity-wall, trophoblast from the time of their first appearance. Hence, while the distinction between polar and mural trophoblast has a clear topographical basis, and though there are distinct differences in the speed with which the two types of trophoblast will undergo further differentiation, there is obviously, in the macaque blastocyst, no fundamental difference in their potentialities. The development of the secondary placenta in the catarrhine monkeys thus demonstrates in a dramatic manner that the abembryonic mural trophoblast of the blastocyst can develop into all of the foetal components of a typical primary placenta. Indeed, in human development, the trophoblast of the abembryonic pole also eventually shows differentiation potentialities identical with those of the embryonic pole. We consider, therefore, that all of the early trophoblast cells of the higher primates possess similar developmental potentialities, though some of them are segregated from the inner cell mass at comparatively late stages in the development of the blastocyst.

In the earliest partially implanted human "ovum" so far described (Hertig and Rock, 1945; Carnegie 8020) the wall of the blastocyst varies from a thin "mesothelioid" membrane at the abembryonic pole to a thick plaque of proliferating syncytium and cytotrophoblast at the embryonic pole. In the equatorial zone of junction between the two areas cells are found which are presumably hypertrophied blastocystic trophoblast, though it is not apparent whether they should be considered mural or polar in origin. At the 9th day (Hertig and Rock, 1945, 1949; Carnegie 8004, 8171), when implantation is nearly accomplished, differentiation into primitive cytotrophoblast and primitive syncytiotrophoblast is much clearer though all stages of transition between these two elements can be identified. We use the term *primitive syncytium* for the *plasmoditrophoblast* of many earlier investigators, for the *plasmodium* of Florian and for the *implantation syncytium* of Grosser. Both primitive cytotrophoblast and primitive syncytium are, of course, derived from the blastocystic trophoblast, either mural or polar. The syncytium, however, is derived indirectly in the sense that it develops from cells which are uninucleate, and which, therefore, cannot initially be distinguished from the remaining cytotrophoblast. Whatever factors are concerned in the differentiation of the syncytium, contact with the endometrium does not appear to be an absolutely determining one for primitive cytotrophoblast can be found in direct apposition to maternal endometrial tissue. Nevertheless, once it has appeared, it is the syncytium which, by phagocytosis and the production of enzymes, is primarily responsible for the local destruction of the maternal tissue. For this reason Mazanec (1959) calls it, at this stage, the *invasion* syncytium.

As development advances the syncytium increases very much in amount. The increase is due in part to growth of the already differentiated syncytium, accompanied by what appears to be amitotic division of its nuclei. In addition, however, the primitive cytotrophoblast, by continuous transformation of some of its cells, often through bizarre transitional stages, also adds to the mass of the syncytium. The boundary between the growing primitive syncytium and the maternal tissues is irregular but gives no impression of a deep penetration of the maternal tissues by foetal elements. By the time the lacunae have developed in the syncytium, however, some definite projections of the latter into the surrounding decidua can be identified. Such extensions consist of multinucleated cytoplasm identical in appearance and staining characteristics with the lacunar syncytium itself.

It is at this stage that localized proliferations of the cytotrophoblast extend into the syncytium, forming the primordia of what will become the primary villi. With continuation of development these villous primordia extend into the increasingly developed lacunar system, which can now be called the intervillous space. During this extension they acquire a thin syncytial covering —the *villous syncytium*—and a mesodermal core. The syncytium is everywhere separated from the foetal mesoderm by cytotrophoblast which, over most of the length of the villi, constitutes a

unicellular layer (*Langhan's layer*; the *central cytotrophoblast* of Ramsey, 1938). At the villous tips, however, rapid proliferation of the cytotrophoblast results not only in the production of solid columns of these cells but also in their extension, from the corresponding villous tips, through the syncytium which separates them from the decidua. In this manner the cytotrophoblast reaches the maternal endometrial stroma. Whether the extension is due solely to cytotrophoblastic proliferation or is, in part, to be attributed to a reversion of portions of the syncytium to a uninucleated state is uncertain. The histological appearances, however, strongly favour the former interpretation for no evidence of a reversion in the syncytium can be seen. When the cytotrophoblast of each column reaches the maternal tissues it spreads laterally in all directions. The extension is due in part to proliferation from the villous tips where mitotic activity is marked. In part, however, it is due to interstitial growth of the trophoblast generally, in which scattered cell divisions are frequently to be seen. The apposition of such extending cytotrophoblastic cells derived from adjacent columns results in the production of the cytotrophoblastic shell which gradually extends round the whole implantation site. The shell consists of a loose aggregation of cytotrophoblastic cells in the midst of which many intercellular spaces or gaps, often of considerable size, can be seen. It is in part, at least, through such gaps in the shell that the blood from the spiral arteries percolates into the intervillous space, since the gaps communicate irregularly with this space.

When the cytotrophoblastic shell is established the original primitive syncytium is separated topographically into two divisions. On the embryonic side of the shell the syncytium, lined by the cytotrophoblastic cells which form Langhan's layer, covers the villi and thus bounds the intervillous space. It is this syncytium which forms the membrane separating the maternal blood in the space from the remaining embryonic tissues and it can be regarded as the definitive placental syncytium. Even in early stages, however, it shows a striking feature the significance of which is not completely understood. This is the appearance, at scattered regions on its surface, of localized areas of proliferation. The resulting small protuberances extend into the intervillous space as what are frequently called the "villous sprouts". Such sprouts are undoubtedly in part the sites of formation of future villous branches. Many of the sprouts, however, never show any development of cytotrophoblast nor is there any formation of a mesodermal core in them. The attachment of such sprouts to the definitive syncytium becomes increasingly attenuated. Eventually many of them separate from the villous syncytium and come to lie free in the intervillous space whence they pass into the uterine veins draining the space and, thus, into the maternal circulation.

The primitive syncytium on the maternal side of the cytotrophoblastic shell is meagre in amount. Small strands of it can be traced amongst the adjacent maternal cells and there is even some tendency to form sprouts closely resembling those just described. Such peripheral sprouts, however, do not usually possess the brush border which is characteristic of many of those found in relation to the intervillous space or to the intercellular gaps in the cytotrophoblastic shell. As development proceeds there is a strong reinforcement to the peripheral primitive syncytium by the differentiation of further syncytium from some of the cells of the shell. As the peripheral syncytium is initially situated in the confusing transitional zone between the foetal and endometrial tissues it is often difficult to be quite certain whether a particular portion of it is a residuum of the initial primitive syncytium or has been recently differentiated from the related cytotrophoblast. The development of the fibrinoid layer called Nitabuch's membrane adds to the difficulty of interpretation. If it is necessary to distinguish between the two varieties of peripheral syncytium on the maternal side of the cytotrophoblastic shell the adjectives *primitive* and *late* sufficiently describe them.

In summary, therefore, the terminology we use for the human trophoblast is essentially a topographical and descriptive one. The whole of the trophoblast of later stages is derived from the blastocystic trophoblast which, during the early stages of implantation, differentiates into syncytium and cytotrophoblast. The former, which for a considerable period receives incre-

ments from the cytotrophoblast, is separated by the development of the cytotrophoblastic shell into two varieties. There is, firstly, an extensive sheet, the definitive syncytium, which covers the villi and lines the intervillous space, and, secondly, there is a much smaller component, the (primitive) peripheral syncytium. This second syncytial component is reinforced later by further differentiation from the cytotrophoblast. The cytotrophoblast shows three divisions. The first of these is the cytotrophoblast of the villi, which, lying between the syncytium and the mesodermal villous cores, constitutes Langhan's layer. Secondly, at the tips of the villi, marked proliferation of the cytotrophoblast produces solid pallisades of this tissue to form the cytotrophoblastic columns. Finally, extension in all directions from the distal (maternal) ends of these columns results in the production of the cytotrophoblastic shell. Later complications, such as the disappearance, if it be a complete disappearance, of Langhan's layer, and the formation of the cytotrophoblastic islands do not affect this classification though, of course, they raise considerable morphogenetic problems. In conclusion, it should be noted that, whereas there is much histological evidence that cytotrophoblast from any of the three divisions described can differentiate into syncytium, there is no good evidence to suggest that the reverse differentiation can occur.

Description

In view of the remarks that have just been made on terminology, the description of our selected stages can be largely restricted to the region of the foetal-decidual junction. On the foetal side this involves, in the earlier implantation stages, only the peripheral syncytium. Later, as will be seen from the description of the individual stages and from the illustrations, the cytotrophoblastic shell comes increasingly to lie directly related to the maternal tissues. Finally, however, the development of Nitabuch's membrane and retrogression of the shell leaves only scattered areas of direct contact of cytotrophoblast with the remains of the decidua.

In the youngest specimen at our disposal (the Barnes ovum, Pl. 1, Fig. 1), with a maximal conceptional age of not more than 12 days, the fully implanted blastocyst possesses an outer wall in which there is already a distinct differentiation into cytotrophoblast and primitive syncytium. The primitive syncytium shows extensive lacunar formation as the preliminary stage in the development of the intervillous space. The surface of the syncytium in contact with the maternal tissues is, in general, regular, but at certain points on its circumference small projections (Pl. 1, Fig. 2) extend for very short distances into the surrounding decidua. The relationship of such masses to the wandering giant cells we shall describe in later stages must remain undetermined. As the illustration shows, the projections are multinucleated and possess a cytoplasm with the granular appearance characteristic of the main part of the syncytium, but they do not possess a brush border. In this specimen the cytotrophoblast has not perforated the syncytium and consequently there is no sign of a cytotrophoblastic shell. The cytotrophoblastic cells are thus completely isolated from the maternal tissues and, on the embryonic side, the maternal-foetal junction is established by syncytium alone. Similar projections have been described by Hertig and Rock (1945) as "blunt pseudopodia" extending out into the endometrial tissue from the somewhat irregularly contoured trophoblast of a 9½-day human embryo. In their description of the 11 and 12-day old specimens, however, these workers (1941) make no specific mention of such projections and the accompanying illustrations do not, in fact, suggest their obvious presence. There may be some variability in this regard in early human embryos.

Through the kindness of Professor R. J. Kellar we have one single section through an implantation site of a human embryo which was obtained during a curettage and which we consider belongs to the late thirteenth day of development. This specimen shows (Pl. 1, Fig. 3), almost diagrammatically, the separation of the primitive syncytium into its two divisions by the cytotrophoblastic shell which is in the process of active formation. Cytotrophoblastic columns are not yet fully established. In the decidua adjacent to the implantation site a number of wandering cells of indubitable tropho-

Plate 1

Fig. 1

Low power view of drawing of the implantation site in the Barnes embryo. ×*c.* 66.

Fig. 2

Photomicrograph of relationship of syncytium to endometrium in the Barnes embryo. Note proliferation of syncytium into the decidua. ×530.

Fig. 3

Photomicrograph of a portion of the implantation site in a *circa* 13-day human pregnancy. Note the beginning of the cytotrophoblastic shell and the presence of young giant cells in the marginal cytotrophoblast and in the decidua. ×170.

Fig. 4

Higher power view of the portion of the implantation site shown in Fig. 5. ×220.

Plate 2

Fig. 5

A portion of the cytotrophoblastic columns and shell and adjacent endometrium of a 28-day human pregnancy. Note the syncytial sprouts in the cytotrophoblastic spaces. Differentiating syncytial streamers from the cytotrophoblast can be traced into the endometrium. ×160.

Fig. 6

Low power photomicrograph of the margin of an *in situ* placenta of a 127 mm. human embryo. On the left of the figure giant cells are seen in both endometrium and myometrium. To the right, beyond the placental margin, giant cells are absent. H. & E. ×32.

Plate 3

Fig. 7

Photomicrograph through the decidua basalis of a 42 mm. human embryo. Large numbers of giant cells are present. H. & E. ×112.

Fig. 8

Photomicrograph showing giant cells in the uterus of a 20-week human pregnancy. H. & E. ×195.

Fig. 9

High power view of the giant cells shown in Fig. 8. Note the appearance of syncytial fusion. H. & E. ×465.

Fig. 10

Photomicrograph of giant cells in a uterus from the second half of pregnancy. Azan. ×200.

Fig. 11

High power view of a portion of Fig. 10. Azan. ×465.

PLATE I

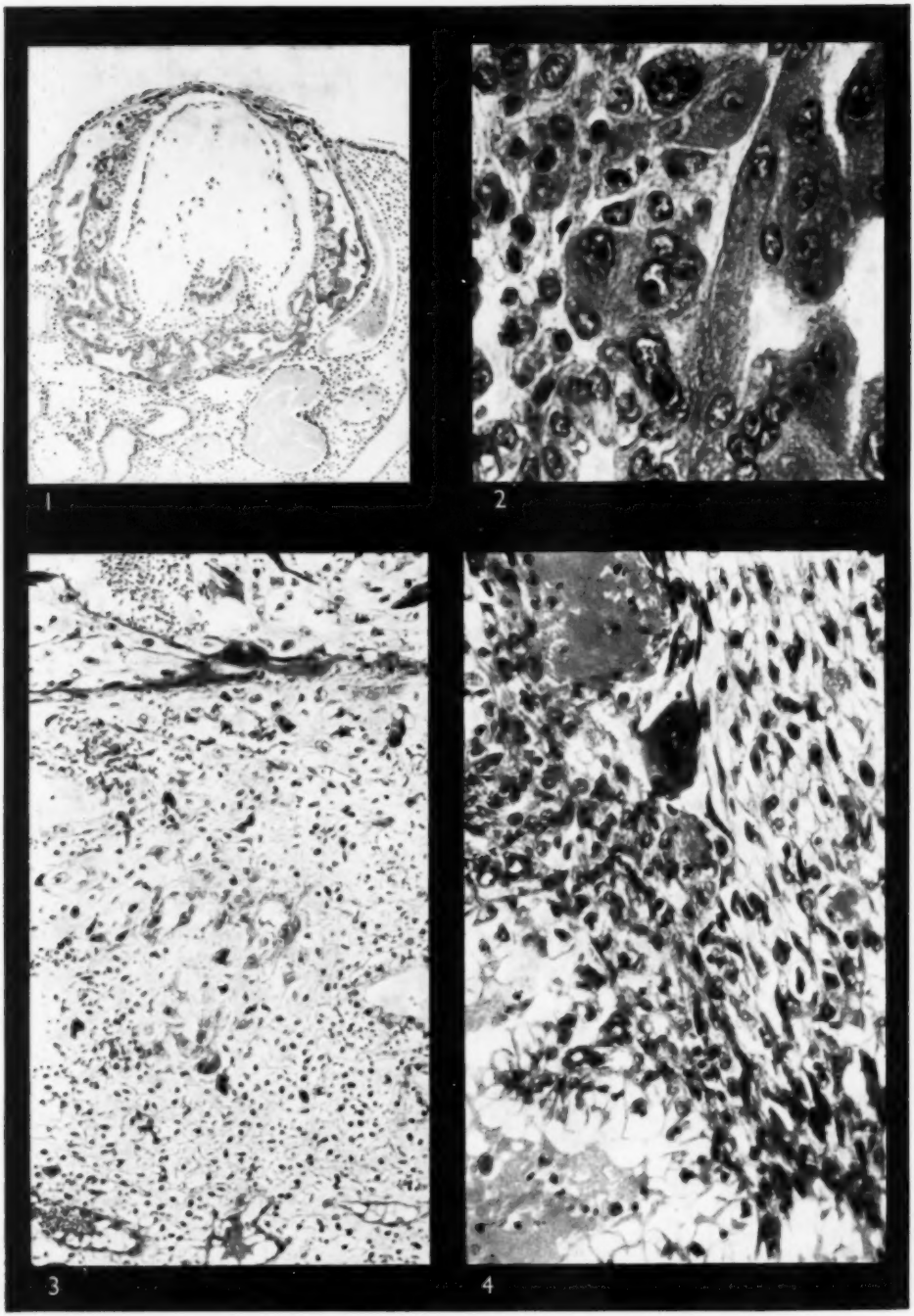


PLATE II

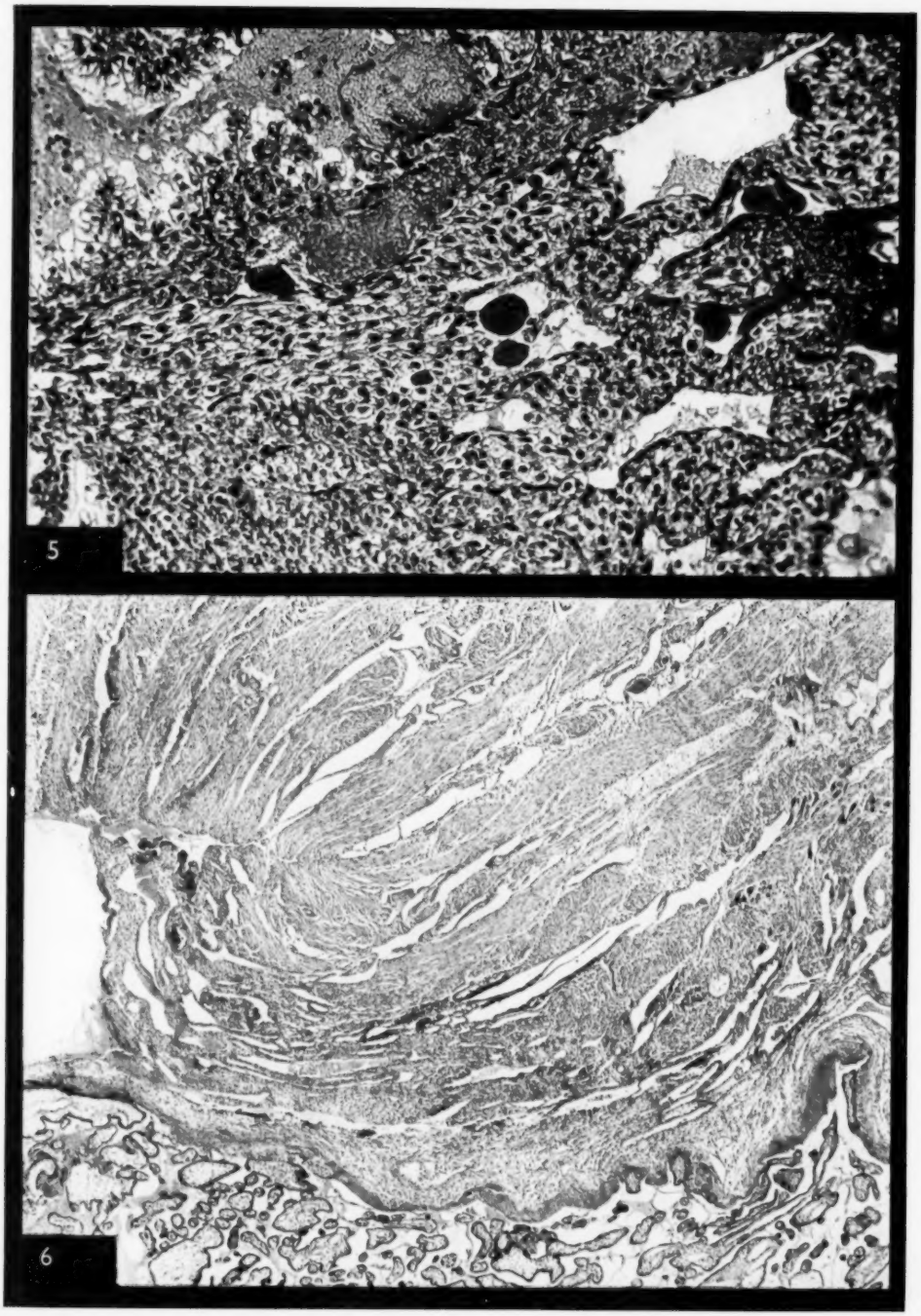
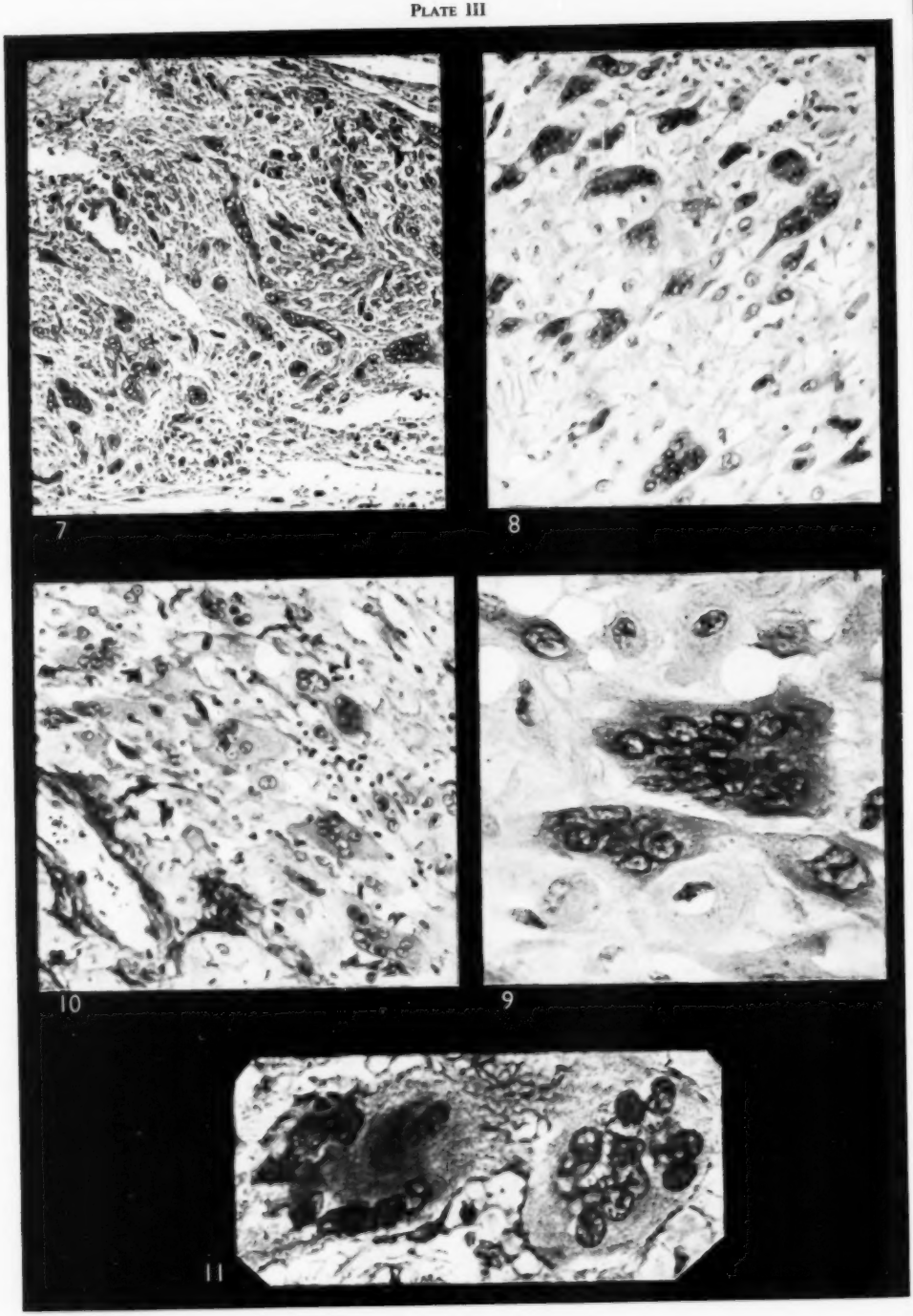


PLATE III



blastic origin are present. They have darkly-staining nuclei and a basophilic cytoplasm which readily enable them to be distinguished from the endometrial cells. They extend out from their origin in the cytotrophoblast into the decidua.

The next three specimens (Missen, Gar, Shaw) available to us for detailed study belong to the period between the fourteenth and eighteenth days of development. We have also, through the courtesy of Professor T. B. Johnston, been able to examine the implantation site of the ovum described by him (1941) and which belongs in the same age group. In all four of these specimens the cytotrophoblastic shell is established and the primitive peripheral syncytium has been separated by it from the definitive syncytium. From the periphery of each of these specimens many syncytial streamers and wandering cells extend out into the endometrium. Some of these streamers are undoubtedly residual remains of the primitive peripheral syncytium itself which may have been forced passively away from the conceptus by the rapid proliferation of the cytotrophoblast of the cell columns and the shell. Most of them, however, in our opinion, are differentiating from the cells of the cytotrophoblastic shell. These can be traced, through transitional stages, from the shell into the decidua where they can be distinguished by their marked basophilia and their elongated shape. In many instances such syncytial elements can be traced directly from the cytotrophoblastic tissue in which they have had their origin. Some of them, however, are quite free from attachment to the shell and these constitute definitely free "wandering" or "migrating" syncytial masses. A variable number of the masses, whether streamers or wandering elements, show a very strong basophilia and a marked pyknosis of their nuclei. The masses presenting these appearances have been interpreted by a number of investigators (see, for example, Krafka, 1941) as being in the process of degeneration. Some of the appearances of degeneration may be associated with the commencing deposition of the fibrinoid substance involved in the development of Nitabuch's membrane; the first signs of this material become apparent in this period. Accounts of peripheral syncytial masses and streamers similar to those described have been given by, amongst others, Peters (1899), Linzenmeier (1914), Falkiner (1932), Brewer (1937), Ramsey (1938) and Heuser *et al.* (1945). From our own observations and the descriptions in the literature we have no doubt that in the third week of human development there is an extensive invasion of the endometrium adjacent to the implantation site by foetal syncytium.

By the end of the fourth week of development (28-somite embryo), the cytotrophoblastic shell has become well established (Pl. 2, Fig. 5). Related to its constituent cells are two varieties of syncytium. In the first place there are multinucleated masses, circular on section, which are often found in the intercellular spaces of the shell. These masses may be residual peripheral primitive syncytium but they are very similar in structure and staining characteristics to the "sprouts" found in relation to the definitive syncytium of the intervillous space. In addition, as can be seen in Pl. 1, Fig. 4, smaller, elongated masses of basophilic syncytium can be seen differentiating from the most peripheral part of the cytotrophoblast. These extend, apparently as migratory elements, into the decidua, but, in many instances, we find it possible to trace protoplasmic continuity between them and the shell. A striking feature of this stage is the presence of a well developed, though discontinuous, Nitabuch's membrane. It is only through the discontinuities in this markedly eosinophilic fibrinoid deposit that the cytotrophoblastic shell is now in direct contact with the decidua.

In all our subsequent *in situ* specimens it is possible to identify foetal syncytium in the maternal tissues adjacent to the developing placenta. Until the time when the basal decidua is reduced in thickness to almost complete disappearance, such masses and streamers of syncytium are found intermixed with the decidual cells. As development continues this syncytium is found gradually to extend into the myometrium overlying the basal placental plate. Indeed, eventually more masses of such multinucleated syncytium are found in the inner part of the myometrium than in the decidua basalis. In this myometrial position the masses frequently become much larger than in the decidua. They

lie in the interstices between the muscle cells where they are often close to, sometimes in direct contact with, the walls of the related myometrial veins. In Pl. 3, Figs. 7 and 8, representative sections at different stages of gestation are illustrated. It must be stressed that we have never observed any signs of transitional stages between the syncytial masses and the decidual or the myometrial cells. On the other hand, we have often been able to trace narrow extensions from these giant cells back towards, or actually to, the cytotrophoblast itself. Meyer (1906) described the migration of the syncytial masses as resembling an Indian file ("*den Gänsemarsch dieser Chorionzellen*") and such an appearance is present in many of our specimens. Owing to the persistence of syncytial strands along the lines of migration it is difficult to be certain whether there is continuous migration of syncytium into the adjacent maternal tissues throughout pregnancy. As the placenta is growing and as, for the first six months at least, the number of giant cells increases, it seems likely that migration from the persisting cytotrophoblast continues for a long period. The late migration is chiefly through gaps in Nitabuch's membrane. In many instances adjacent syncytial masses are joined to each other by delicate strands (Pl. 3, Fig. 9); but we are unable to decide if this is a true secondary fusion of initially separate masses or the result of branching of independent units.

It must also be stressed that such cells are found only in relation to the endometrium and myometrium overlying the placental site (Pl. 2, Fig. 6). As one passes towards the peripheral margin of the placenta the syncytial masses decrease in number and usually disappear before the margin itself is reached. That is to say they are not found in the decidua vera or in the myometrium overlying it. We have never, in any of our large number of specimens, found syncytium in the maternal tissues of the uterus beyond the margin of the placenta itself. Teacher (1935) has also drawn attention to the topographical localization of the giant cells. He writes: "A characteristic feature of the placental site is the presence of the chorionic giant cells which are absolutely confined to this area."

It can also be stated quite categorically that such giant cells are present in all of our specimens. They are most numerous in specimens from the middle of the gestation period but large numbers are present at, or near, full term. Indeed, giant cells are still to be found in post-partum uteri up to as late as the sixth day of the puerperium. Sharman (1953) has also recorded giant cells as being present until the fifth day post-partum but he considered them to be of decidual origin.

With routine haematoxylin and eosin staining the syncytial masses can be readily distinguished from decidual cells (Pl. 3, Fig. 9). They are multinucleate, very irregular in shape, and may be as large as 300μ in one or more dimensions. The nuclei are often darkly-staining though occasionally larger and more palely-staining ones are found. Their cytoplasm is also basophilic and has a coarse texture which is extremely similar to that of the primitive syncytium (cf. Pl. 1, Fig. 2 and Pl. 3, Fig. 9). With the Masson trichrome technique the cytoplasm of the syncytium stains a dark violet in marked contrast to the decidual cells. When Heidenhain's Azan technique is used the syncytial cytoplasm is stained a much deeper orange colour than is that of the decidual cells (Pl. 3, Figs. 10 and 11). In none of our material were elements transitional in staining characteristics between those of the maternal cells and those of the giant cells found.

Discussion

In view of the findings recorded in this paper the question at once arises: "why is there doubt about the nature of these giant cells?" Hinselmann (1958), in a recent review of the giant cells, states that, in his opinion, they have been treated in a "step-motherly" fashion. And, indeed, they have not been given the attention they deserve. Part of the lack of attention to them has been due to the absence of liaison between the early stage embryologists and those who are interested in the mature placenta.

A large number of investigators, notably Kastschenko (1885), Webster (1901) Meyer (1906) and Schiller (1922), have studied the giant cells in the later stages of pregnancy and have attributed a foetal origin to them. Others, however, for example, Keiffer (1928), have argued

strongly against such an origin, believing that they are of maternal origin. Keiffer studied only small portions of the uterine wall removed at operation and in view of the lateness of the stages available to him and the limited regions studied it is difficult to understand his dogmatism. Material removed by curettage also seems to us to be unsuitable for a solution of the problem. With *in situ* specimens from selected stages of pregnancy, however, the whole history of the giant cells becomes quite clear, and the gap is bridged between the observations of embryologists, who have been chiefly interested in the early stages of implantation, and those of the obstetricians and pathologists who have been concerned mostly with material from the later stages or from curettages. Indeed, many embryologists have already given completely convincing accounts of the outward migration of the early syncytium and of the relation of this migration to the giant cells of later stages. Thus, Peters (1899) and Graf Spee (1915) gave good accounts of the process. Falkiner (1932) and Ramsey (1938) have given more recent critical discussions in relation to descriptions of the implantation sites of young embryos. The observations of these and many other investigators (see Grosser, 1927, for discussion) leave little doubt about the reality of the syncytial migration into maternal tissue. Any remaining doubts will be readily removed by examining the well-fixed implantation site of a young human embryo.

In spite of this certainty on the earlier stages there remain the doubts, such as have been expressed by Park (1959) and which are referred to in the introduction to the present contribution, about the relationship of the early migratory strands to the impressive giant cells associated with the fully-established placenta. When, however, placentae at closely spaced time intervals during pregnancy are examined the phenomenon of outgrowth of syncytial elements into the maternal tissues becomes an impressive one. The continuity which many of the giant cells show with the basal plate trophoblast and their histochemical similarities to this tissue (McKay *et al.*, 1958) indicate quite definitely their foetal origin. We have tried to "sex" the syncytial streamers and giant cells from their nuclear structure using the now well-known technique based on the investigations of Barr and his associates. As we know, in most cases, the sex of the embryos and foetuses associated with our *in situ* placentae, the absence of the female pattern of sex chromatin in the nuclei of the giant cells associated with the placentae of male foetuses would be a final proof of the validity of the contention that the masses are of foetal origin. Unfortunately, however, it has not been possible in the multinucleated syncytial masses, with heavily staining nuclei, to be certain about nuclear sex. This final proof is, therefore, still beyond us, but even without it we consider that the developmental history of the giant cells makes inevitable the conclusion that they are of foetal origin.

The constancy with which the giant cells are present, their large numbers and the remarkable appearances presented by their cytoplasm and nuclei all suggest an important function. Their existence in the midst of the maternal tissues also raises the problem as to why they are immune to a homograft reaction. The persistence of such foreign cells in the uterine endometrium and myometrium, and their normal continued presence for some undetermined period after parturition, also raises problems of pathological interest.

Possible functions for the giant cells are the production of enzymes, which might "soften up" the maternal tissues, and the elaboration of hormones. The "softening up" could enable placental growth to take place and might conceivably help in establishing a cleavage plane for eventual placental separation. We have the impression, however, that there is no marked local effect, cytolytic or otherwise, of the giant cells on the maternal tissues. They appear to push aside the maternal cells and to dissolve the surrounding reticulin and collagen (as is shown by reticular stains and Light Green) but there is no appearance of a very active destructive effect on the adjacent maternal cells. Indeed, there would appear to be distinct disadvantages arising from the presence of giant cells with much cytolytic activity in the myometrium.

We, therefore, incline to the view, already expressed by Keiffer (1928), that the histological appearances suggest the possibility that these foetal syncytial masses are concerned in the

production of a hormone. Latta and Beber (1957) have also made this suggestion for the "cells" they found in relation to the basal plate of the separated placenta. From their histochemical observations they suggested that these elements may be secreting gonadotropin and ACTH. We, ourselves, are not yet prepared to make a statement on the nature of the secretion of the giant cells, if they do, in fact, possess one. Our findings, however, make it possible to write that investigations on separated placentae whether by histology, histochemistry, tissue culture or perfusion, do not permit the study of the giant cells. This fact, of course, explains why Wislocki and Bennett (1943) and Dempsey and Wislocki (1944) in their classical descriptions of the histology of the human placenta pay no special attention to syncytium remote from the actual area of attachment. A separated placenta does not possess all the products of trophoblastic differentiation. Conversely, removal of the placenta does not immediately exclude all possible sources of influence, hormonal or otherwise, of foetal tissue on the maternal organism. There are, in fully established pregnancy, many thousands of the giant cells overlying the basal plate, and each of them (or, when they are partially fused, several of them together) represents a considerable volume of cytoplasm. Collectively they form a mass of foetal tissue which could have considerable biological activity and which certainly cannot be disregarded in any assessment of trophoblastic function.

There are two other extensions of trophoblast into the maternal organism which should perhaps be mentioned here, though we consider that they are phenomena quite different from that which results in the production of the giant cells. In the first place there is an extension of cytotrophoblastic cells for considerable distances up the spiral arteries in the first half of pregnancy (Boyd, 1956; Boyd and Hamilton, 1956, and in press). This extension may be related to the opening up of these vessels and it may also help to reduce the arterial pressure before discharge of the maternal blood into the intervillous space. Secondly, there is the remarkable phenomenon of the liberation of syncytial "sprouts" into the maternal veins and thence to the lungs (Schmorl, 1893; Veit, 1905; Park, 1958; Boyd, 1959; Thomas, Douglas and Carr, 1959).

The presence of migratory foetal elements is not confined to the human placenta. There is now a voluminous literature dealing with them in many mammalian species and there are conflicting views as to their origin. Many of the earlier investigators (Hubrecht, 1889; Duval, 1892; Jenkinson, 1902; Sobotta, 1903; Andresen, 1927) had no doubt of their trophoblastic derivation. Others, such as Disse (1906) and Sansom (1922), believed in their maternal origin. Recently, Wimsatt (1951) and Björkman (1954) have given detailed accounts of the origin and history of these cells in ruminants and are definitely of the opinion that they arise by differentiation from the cellular trophoblast. Orsini (1954) has described and classified these giant cells in the hamster and she also concludes that they are derived from the trophoblast. Davies and Halmi (1953) have suggested that at least some of the giant cells of the abplacental region in the rabbit are of myogenic origin. It may be that some of the syncytial masses found in other mammals are in fact of maternal origin and that such cells are not homologous to the human placental giant cells. Even in as high a primate as the macaque monkey Wislocki and Streeter (1938) have described endometrial syncytial masses which they considered to take origin from the maternal epithelial plaque. In the course of the development of the human placenta, however, we have, ourselves, been able to identify no signs of a maternal contribution to the giant cells.

Summary

(1) The terminology for the human trophoblast is reviewed.

(2) The penetration of maternal endometrium and myometrium by foetal syncytium is described.

(3) It is concluded that the giant cells of the human pregnant uterus are all derived from this foetal syncytium. In over 100 *in situ* placentae from all stages of gestation no evidence was found to suggest a maternal origin for the giant cells.

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BRAIN DISEASE IN STILLBORN INFANTS AND NEONATES

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INTRODUCTION

UNDER the auspices of the National Birthday Trust Fund, a perinatal mortality survey on a national sample of stillbirths and neonatal deaths was carried out in March, 1958, with the purpose of correlating clinical and pathological data. The infants were brought to centres for detailed morbid anatomical and histological examination.

A number of brains, spinal cords, eyes and pituitaries were made available for study from one region, the South-West Metropolitan Hospital Region. The material was collected at Queen Charlotte's Maternity Hospital and studied at the Fountain Hospital. The necropsies were done by Dr. A. E. Claireaux, and the central nervous systems examined by Drs. L. Crome and P. E. Sylvester.

The purpose of this paper is to report the main pathological findings and to correlate them with clinical data. Emphasis is made on the findings in the nervous system, but significant findings in other systems are included. Later it is planned to report the relation to specific aspects of neonatal morbidity.

MATERIAL

Necropsies in 101 infants were carried out, and of these, 58 or 57·4 per cent (33 males and 25 females) were stillborn and 43 or 42·5 per cent (27 males and 16 females) were born alive and survived periods varying from 10 minutes to 31 days. Thirty-one or 30·7 per cent, infants were macerated. From this source 70 brains, 59 spinal cords, 44 pairs of eyes and 6 single eyes, and 48 pituitaries were obtained for more detailed anatomical and histological study.

The survey was not confined to infants born in hospitals, although most came from that source, but extended also to those born at home or in private Nursing Homes.

The birth rate in the South-West Metropolitan Hospital Region which serves a population of 4,954,320 was not available for this report but figures for the London Administrative County Area which adjoins and forms a part of the Region were available for 1957 (General Register Office, 1958). The population of the London Administrative County Area was 3,254,000 at that time, and the birth rate 16·2 per 1,000 total population. The stillbirth rate was 20·1 per 1,000 live births and the neonatal mortality 16·3 per 1,000 live births.

METHODS

Each body was weighed on a heavy duty balance and the crown-rump, crown-heel and head circumference measured. Individual organs were weighed on a compression balance and pieces retained for histological processing. Bacteriological studies were carried out where indicated. The placenta, when available, was weighed and studied both macro- and microscopically.

The scalp was deflected from the skull after a coronal incision. Two incisions were made, one on each side of, and parallel to, the sagittal sinus and carried along the soft coronal and occipital-parietal sutures so that, by this means, the frontal and parietal bones, with the dura, could be peeled away from the brain. In more mature brains, it was necessary to break forward the frontal bone after making a horizontal saw

incision 2 cm. above the orbits. Because the superior sagittal sinus was preserved by this method of exposure, it was possible to view the hemispheres with the minimal amount of false bleeding created by necropsy trauma; the sagittal sinus and falciform ligament could also be studied. The falciform ligament could be deflected posteriorly after dividing its frontal attachment. The brain was then rocked gently first to one side, then the other, in order to examine the tentorium. Gravity was allowed to displace the brain from the anterior, middle and posterior fossae. It was collected into a flat scale pan and handling was excluded as much as possible to avoid damage to the organ. A note was made of the state of the straight sinus and the vein of Galen.

The water content of 40 fresh brains was estimated by removing the tip of one occipital lobe and weighing before and after dehydration. For this a semi-micro analytical balance was used, and weighing continued until a constant weight resulted. This was achieved after 12 hours dehydration at 110° C.

Fixation was carried out in 10 per cent formaldehyde solution (B.P.) in normal saline, which was the fixative used for all tissues.

After fixation, the brains and cords were re-examined. Radiographs were taken of 53 brains. Each brain, with brain stem and cerebellum, was re-weighed on a heavy duty balance and measured. Notes were made of the symmetry and gyral pattern of the brain, and also the state of the cranial nerves and blood vessels. External pathological features were recorded. The brain stem with the cerebellum were then removed and weighed separately, and the hemispheres were separated. Coronal sections were made through each cerebral hemisphere and representative sections taken for celloidin embedding. Blocks of the mid-brain, pons, medulla, cerebellar hemisphere were also embedded in celloidin. The cerebral hemisphere and brain stem of a number of brains were processed by the Weigert-Pal technique.

The spinal cord in its dural sheath was weighed on a heavy duty balance and its length, from the point of severance from the medulla to the beginning of the filum terminale, measured by a steel rule. Representative sections were taken from the cervical, thoracic and lumbar levels and embedded in celloidin. Sections from some cords were processed by the Weigert-Pal technique.

The eyes were removed through the orbital roof after removing the bone and injected with formalin before being placed in formalin fixative. Subsequently, various diameters of the globes were measured and later, after freezing in a mixture of 64 O.P. methylated spirit and solid CO_2, they were bisected, allowed to thaw, and a naked-eye comment on their internal structure made before embedding.

Pituitaries, after removal, were fixed in formalin and later trimmed to remove unnecessary tissue. A number (33 out of 48) were weighed on a general laboratory balance.

Results

Sixty-two infants (61·3 per cent) had abnormalities of the brain. Haemorrhages involved the nervous system in 44 cases (43·7 per cent); 2 of these were macerated. Ten infants (10 per cent) had congenital malformations; 6 of these had anencephaly, 2 Arnold-Chiari malformations and 2 hydrocephalus. There was considerable under-development (poor gyral formation and opercular defect) in 17 infants' brains (16·8 per cent) but 11 of these also had haemorrhages and have been included in the haemorrhagic group. One infant died of staphylococcal meningitis and one child had an extension of a pharyngeal teratoma into the frontal lobe.

In 39 infants (38·7 per cent) no comment has so far been made. Ten of these were well preserved infants with normal looking brains. Twenty-nine infants were macerated and comment on their nervous systems thereby limited. A scattergraph of the weights of the brain in relation to body weight is shown in Figure 1, and the correlation between the weights of the whole fixed brains and their cerebelli shown in Figure 2. Pathological features did not upset the expected relationship.

The mean water content of 40 brains determined by Dr. J. Stern, was 89·0 per cent, standard deviation 1·85, range 85·9 per cent–93·7 per cent.

The mean weight of 33 pituitary glands was 0·102 g., standard deviation $\pm$0·038 g., range 0·04–0·17 g.

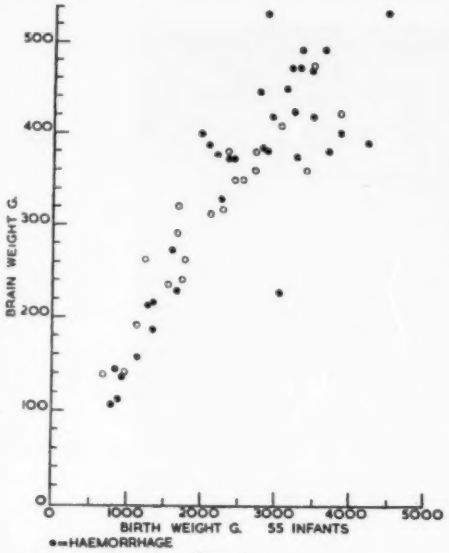

FIG. 1

Relationship of brain weight to birth weight of 55 infants.

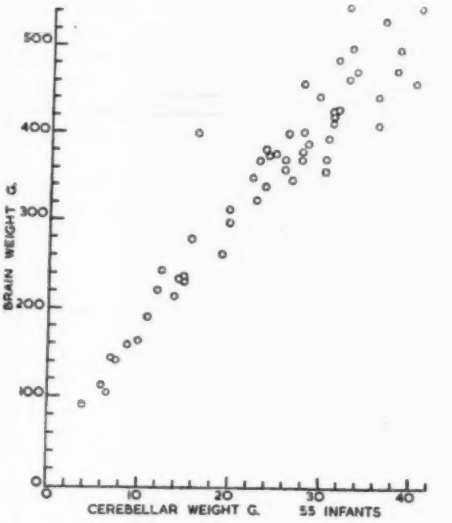

FIG. 2

Relationship of brain weight to cerebellar weight of 55 infants.

Of the 53 brains, including 4 anencephalics, which were radiographed, only one showed evidence of calcification—the one with a teratoma in the frontal lobe. Four had dilatation of the ventricles. This was slight in one brain—from the child with staphylococcal meningitis, and severe in the other 3—one of which was from a hydrocephalic infant, one from the infant with the frontal lobe tumour and one from a child with achondroplasia.

Forty-four pairs of eyes were examined and bleeding was seen in 10 cases in the following places:

Retina	5
Vitreous	2
Perilimbal	2
Perilenticular	1

The haemorrhages were either small, multiple discrete pinpoints, or larger, in which case they were crescentic.

It was considered convenient to present the cases in two groups, namely: (*a*) premature infants, and (*b*) mature infants.

(*a*) *Premature Infants.* There were 56 premature infants, i.e., with birth weights of 5 pounds 8 ounces (2,500 g.) or less. Haemorrhages involved the nervous system in 19 infants (14 males, 5 females). Twenty infants (13 males and 7 females) with a mean birth weight of 1,567·3 g. were macerated (18 were macerated stillbirths and 2 showed post-mortem autolysis).

As expected a number of infants (17; 11 males, 6 females) had brains with incomplete external formation. With a mean birth weight of 1,249 g. (range 820–1,670 g.) they were the lightest infants in the series. All their brains had incomplete closure of the operculum with exposure of the insula. The smaller the infant the simpler was the pattern of the external formation of the brain. For instance, 2 infants whose mean birth weight was 806 g. had brains in which primary, secondary and tertiary sulci were absent (Fig. 3); 11 infants whose mean birth weight was 1,226 g. had primary but no secondary or tertiary sulci (Fig. 4): and 3 infants, with a mean birth weight of 1,623 g. had brains with primary and secondary but no tertiary sulci (Fig. 5). By contrast, 12 infants (7 males, 5 females) whose mean birth weight was 2,190·9 g. had brains in which

TABLE I

An Analysis of Clinical Features of 49 Premature Infants and Foetuses

State of Brain	No. of Cases	Maternal Age Range (mean) Yrs.	Term Range (mean) Wks.	Birth Weight Range (mean) grams	Maternal Health				Antepartum Haemorrhage	Presentation		Live birth	Stillbirth
					Good	Toxaemia	Hyperemesis	Unknown		Vertex	Breech		
Complete external configuration	12	18–34 (25·3)	33–42 (37·7)	1,725–2,495 (2,190·9)	6	2	2	1	3	9	1	9	3
Incomplete external configuration	17	21–37 (26·5)	23–38 (29·1)	675–1,670 (1,249·4)	14	2	0	0	11	7	9	14	3
Macerated	20	19–38 (30·5)	29–40 (35)	680–2,380 (1,568·3)	8	7	1	2	4	12	4	2	18

In addition one of the mothers who had a macerated infant had chronic nephritis and one mother who had an infant with incomplete external configuration had had congenital syphilis.

the external configuration was comparable with that of a full-term mature infant. It was convenient to keep these two groups separate so that comparison could be made of the pathological findings in them.

Table I summarizes the clinical details of the premature infants. Two infants with primary sulci but absence of secondary and tertiary sulci had congenital anomalies. In one infant there was wide patency of the tentorium, which had allowed herniation of the temporal lobes so that deep linear grooves had formed across the tips of the lobes. In the other child's brain the septum pellucidum was absent.

One infant had a sessile calcified tumour (4·0×3·0 cm.) in the right frontal pole which was an extension of a teratoma from the nasopharynx. Though soft and distorted the remaining parts of the brain appeared to have formed normally on external examination, but there was considerable dilatation of the ventricular system.

Anencephaly affected 6 infants (3 females, 3 males) and as they are to form part of a special study they will not be considered further in this report.

The sites of bleeding into the nervous system are compared with those in the mature infants and summarized in Table II. Ventricular bleeding

TABLE II

Comparison of the Presentations, Deliveries and Sites of Bleeding into the Nervous System in Mature and Premature Infants

	Presentation				Delivery			Bleeding							
	Vertex		Breech		Spontaneous	Forceps	Caesarean Section	Lesions of Vein of Galen	Dural Tears	Subarachnoid	Ventricular	Parenchymal	Subdural	Spinal Cord	Eye
25 Mature infants	19		6												
	Stillbirths 7	Live births 12	Stillbirths 5	Live births 1	11	12	2	3	7	16	0	4	11	9	6
19 Premature infants	10		9												
	Stillbirths 1	Live births 9	Stillbirths 3	Live births 6	15	3	1	3	3	7	6	3	4	2	0

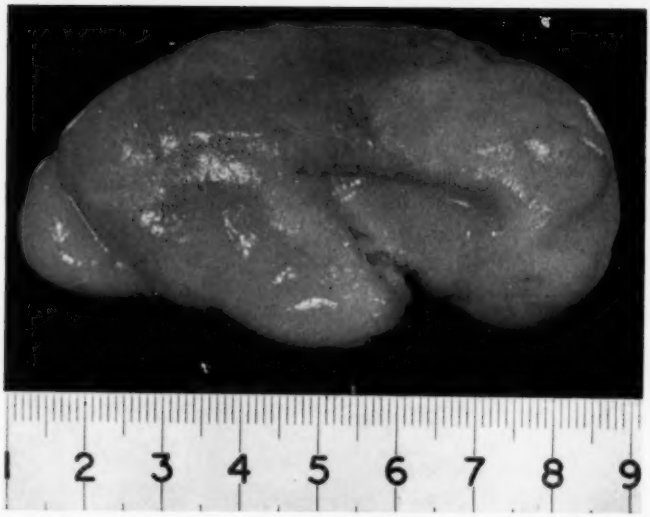

FIG. 3

Absence of sulci and wide opercular defect in the brain of an infant whose birth weight was 675 g.

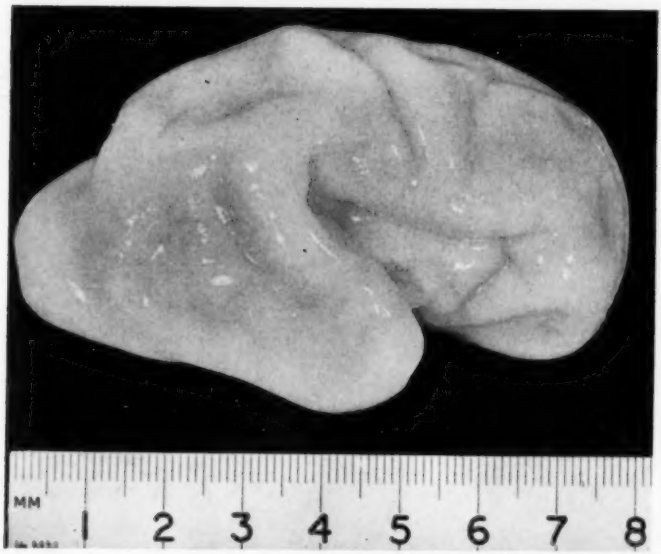

FIG. 4

Primary sulci defined but secondary and tertiary sulci absent and wide opercular defect in the brain of an infant whose birth weight was 792 g.

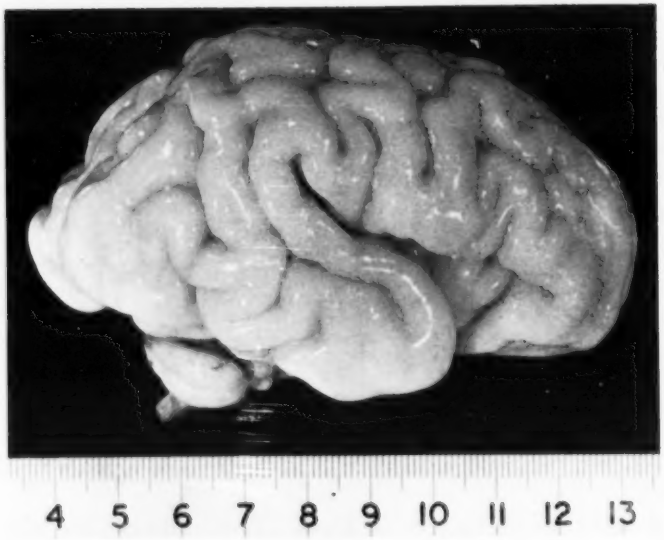

FIG. 5

Primary and secondary sulci defined but tertiary sulci absent and opercular defect in the brain of an infant whose birth weight was 1,725 g.

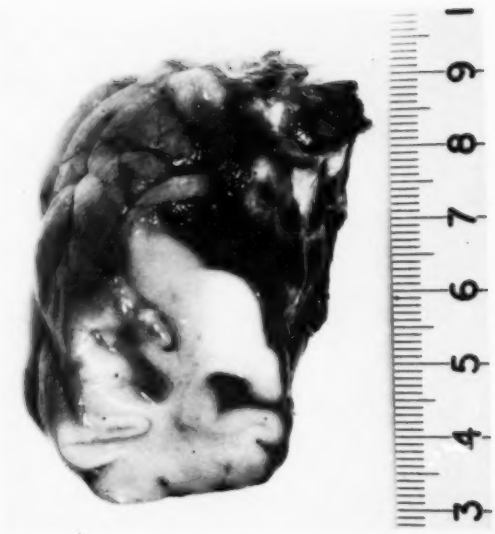

FIG. 6

A portion of the left occipital lobe of an infant, whose birth weight was 3,175 g. Part of a large subdural haematoma (7·0×4·0×1·0 cm) (removed) lay over the darkly stained vertex and medial surface. There was extensive softening of grey and white matter of the opposite perimeter of the lobe. Blood clot was present in the post-calcarine sulcus.

was confined to the smallest sized premature infants. The findings varied slightly in each case, for instance:

(1) Blood was present in the cerebello-pontine angles, the cisterna magna and inter-peduncular fossa. There was a large blood clot over the left terminal vein from which it appeared bleeding originated. Blood clot was present in both lateral ventricles, including the posterior horns, and in the aqueduct.

(2) Haemorrhagic fluid was present in the left posterior horn.

(3) There was blood inside the cisterna magna and over the left cerebello-pontine angle. There were many periventricular haemorrhages around the anterior part of the left ventricle—the adjacent brain tissue being very soft. The ventricles were slightly but definitely dilated. Posteriorly there was bleeding into both ventricles. A flame-shaped haemorrhage was present in each corona radiata. The fourth ventricle contained blood.

(4) Blood clot was present in the left lateral ventricle.

(5) The left lateral ventricle of a brain with obstructive hydrocephalus due to stenosis of the aqueduct contained a clot (1 cm. diameter) which probably arose from the terminal vein.

(6) Blood clot was found in the third, lateral and fourth ventricles but there was no intracerebral haemorrhage.

The causes of death amongst the premature infants are shown in Table III.

(*b*) *Mature Infants.* There were 45 infants in this group. Haemorrhages involved the nervous system in 25 (16 males, 9 females), 19 were macerated (8 males, 11 females) and of these 12 were born macerated and 7 showed post-mortem autolysis. One which did not fit into either of these groups had severe malformation of the heart.

Two infants amongst those with haemorrhages, had severe Arnold-Chiari malformations, with gross internal hydrocephalus and spina bifida cystica in the lumbo-sacral regions. One child had a diastematomyelia. It had been necessary to aspirate C.S.F. through the spina bifida in each case to assist delivery—40 ounces (1,120 ml.) in the one case and 45 ounces (1,260 ml.) in the other.

The location of bleeding and clinical details are summarized and compared with those in the premature infants in Table II.

Lesions of the vein of Galen included thrombosis in one case in whom a large subdural haematoma extended over the vertex of the left hemisphere (Fig. 6). Extensive softening affected

TABLE III

The Cause of Death Amongst 56 Premature Infants

	State of Brain		
	Complete External Configuration	Incomplete External Configuration	Macerated
Intra-partum anoxia	2	5	15
Prematurity with atelectasis	1	0	1
Congenital malformations of the heart ..	2	1	1
Pneumothorax and emphysema	2	0	0
Pulmonary hypoplasia	0	0	0
Atelectasis with hyaline membrane	3	5	0
Intraperitoneal haemorrhage	0	1	0
Intrapulmonary haemorrhage	2	2	0
Intraventricular haemorrhage	0	2	0
Subarachnoid haemorrhage	0	1	0
Subdural haemorrhage	1	0	2
Haemolytic disease	1	0	1
Meningitis	0	1	0

both grey and white matter at the opposite perimeter of the hemisphere. The causal relationship of the thrombosed vein to the haematoma was not clear. In the other 2 cases, the vein was lacerated and in one, without tentorial tearing, a subdural haematoma had formed in the region of the tear; the other child had an associated dural tear with a haematoma in the posterior fossa; in this child there was also a haemorrhage over the right temporal and occipital regions.

In the 7 instances where the tentorium was lacerated, there had been severe subdural bleeding. In most cases the blood had tracked into the middle fossa and from there over one or other hemisphere; in one case blood had tracked into the posterior fossa. The lateral sinus, the base of the falx, the straight sinus and the vein of Galen were involved by the tears in one instance each. The tears were bilateral in 3 cases.

Subarachnoid bleeding varied greatly in its extent. In some instances small, often multiple, discrete haemorrhages were present; in others, larger map-like areas had formed, whilst in some blood had trickled along the course of the sulci. Table IV illustrates their disposition.

TABLE IV

The Sites of Subarachnoid Bleeding Amongst 24 Infants

	R.	L.
Vertex	7	6
Sylvian fissure	2	3
Frontal lobes	0	2
Temporal lobes	3	3
Occipital lobes	3	4
Cerebellum	5	7
Pons	3	3
Cisterna magna	2	2

There were 11 instances of haemorrhage involving the spinal cord.

Death in infants with bleeding into the nervous system was attributed to the causes in Table V.

Fifteen of the children in this group had aspirated meconium. Death was attributed to intra-partum anoxia in 16 cases, to congenital malformations in 2 cases and post-operative and following haemorrhage from a torn placenta in 1 case each.

TABLE V

The Causes of Death in 44 Infants with Bleeding into the Nervous System

	Pre-mature	Mature
Intra-partum anoxia	2	8
Prematurity with atelectasis	6	0
Congenital malformations	2	6
Intrapulmonary haemorrhage	4	3
Pneumothorax and emphysema	3	0
Pulmonary hypoplasia	1	1
Atelectasis with hyaline membrane	6	2
Intraperitoneal haemorrhage	1	1
Subdural haemorrhage	3	10
Intraventricular haemorrhage	2	0
Subarachnoid	1	0

Intra-partum anoxia could not always be explained, but in some cases there seemed to be an obvious cause. In 2 cases there had been retroplacental bleeding; severe ante-partum haemorrhage occurred in another case just before the onset of labour and led to placental insufficiency; in another child there was a true knot in the cord.

In one infant who lived 2 days there was a tentorial tear on the right side but intracranial haemorrhage was absent.

The ages of the mothers of the infants with bleeding ranged from 21 to 43 years (mean 30·5 years), in whom general health during pregnancy had been good in 12. Six had toxaemia of pregnancy; one of these mothers was mentally defective. Two had urinary tract infections whilst heart disease, pulmonary tuberculosis and influenza affected one mother each. Two mothers in good health and the one who had influenza had ante-partum haemorrhages. Miscarriages were not reported in any mother. Eleven mothers had not been pregnant previously, 3 had had one previous pregnancy, 1 had 2, 3 had 3, and 4 mothers had respectively 4, 5, 9 and 11 previous children. The earlier obstetrical history was unknown in 2 mothers.

The ages of the mothers of the 19 macerated infants ranged from 17 to 40 years (mean 31 years), in whom the general health had been good in 12. Four had toxaemia of pregnancy. Influenza and epilepsy affected one mother each,

TABLE VI

	Incidence of Haemorrhage (Neonatal and Stillborn) Per cent	Haemorrhage as Cause of Death Per cent
Capon (1922)	37·5 (30 out of 80 cases)	—
Arey and Dent (1953)	—	12·0
van Dongen (1956)	—	8·7 (23 out of 206 cases)
Haller *et al.* (1956)	—	9·0 (94 out of 1,043 cases)
Claireaux (1959)	19·8 (209 out of 1,056 cases)	12·3 (131 out of 1,056 cases)

and in one mother the state of her health was unknown. Three mothers in good health had ante-partum haemorrhages. Two mothers had previous miscarriages. Four had not been pregnant before, four had one, four two, one three, three four, one five, one six, and one seven previous pregnancies.

DISCUSSION

The incidence of haemorrhage involving the central nervous system in the stillborn and neonatal infants of this series was 43·7 per cent (44 cases out of 101) and was considered to be the cause of death in 15·8 per cent (16 cases out of 101).

In Table VI these figures are compared with those of other observers.

The presentation and method of delivery appeared to have a significant association with nervous system bleeding, for instance, the incidence of breech presentations (see Table II) was 34·2 per cent and was similar to the incidence of 30·9 per cent given by Haller, Nesbitt and Anderson (1956). These incidences are ten times the average incidence of breech presentations (3·3 per cent) given by Brews (1948) for all deliveries. In this series, the incidence of forceps deliveries was 48 per cent, which was almost twice the figure found by Haller, Nesbitt and Anderson (1956), viz., 25·7 per cent.

Haller, Nesbitt and Anderson (1956) and Claireaux (1959) divided intracranial haemorrhages into two categories, those caused by birth trauma and associated with dural tears and subdural bleeding, and those caused by anoxia and associated with intraventricular parenchymal and subarachnoid haemorrhages. Both groups could be identified in the present series. A comparison between the premature and mature infants to determine whether there was any significant difference in these two groups in the incidence of anoxic and traumatic bleeding failed to reveal a significant difference in the chi-squared test: $\chi^2 < 1{\cdot}074$ (one degree of freedom), $P > 0{\cdot}3$. However, similar comparison applied to the premature infants between those with incomplete and complete external brain formation indicated, that, while there were too few cases to apply a chi squared test, there was probably a significant incidence of anoxic haemorrhage amongst those infants with incomplete external brain formation, for instance, 11 instances of anoxic and none of traumatic bleeding. Whereas, there were 2 cases of anoxic and 4 of traumatic bleeding amongst those infants with complete external formation.

Ten of the 11 instances of spinal cord haemorrhage (9 mature, 2 premature infants) were associated with vertex presentations. The remaining infant born by a difficult breech delivery and with a fracture-dislocation of the twelfth thoracic vertebra was the only instance of bony injury in the series. Six infants were born spontaneously, 3 required forceps assistance and 2 were delivered by Caesarean section. Anoxic type of intracranial bleeding was found in 5 infants (in one of these it was considered that

TABLE VII

Placenta/Body Weight Ratio in 35 Infants With and Without Meconium Staining

	With Meconium Staining	Without Meconium	Significance of the Difference by Student's t-test
Mature	mean 0·171 (12 cases)	mean 0·218 (10 cases)	significant at the 0·02 level
Premature	mean 0·238 (4 cases)	mean 0·304 (9 cases)	not significant

blood had extravasated down over the cord and along the sheaths of nerve roots from the intracranial bleeding); traumatic brain haemorrhages occurred in 2 infants and combined types of bleeding in 1 instance. Intracranial bleeding was absent in 3 cases. In most instances bleeding involved the cervical and thoracic levels but it was found in the lumbar region in one child. Bleeding was epidural in 7 cases, subdural in 3, and into the substance of the thoracic cord in one.

Some infants were reported to suffer from either white or blue asphyxia at birth, but as information was incomplete on these points, the presence of meconium in the liquor was taken as the indication that foetal distress had existed. The greatest incidence of this was in the macerated group of mature infants—17 cases (90·5 per cent); next, in the mature infants with bleeding into the nervous system—10 cases (40 per cent). By the classification of Claireaux and Haller *et al.*, 7 infants in this last group had anoxic brain haemorrhages, 2 had traumatic haemorrhages and in 1 case combined lesions were present. Premature infants had the lowest incidence, for instance, in the premature infants with brains of complete external formation—1 case (8·3 per cent), those with brains of incomplete external formation—3 cases (17·7 per cent) and those with macerated brains—3 cases (15 per cent). There were no instances of cerebral bleeding amongst the premature infants with meconium-staining. Fifteen of the macerated group of mature infants were born spontaneously by the vertex, without complications of labour or delivery. This contrasted with the group of premature infants with intracranial haemorrhages but without meconium-staining, in whom 9 of the 19 were born by the breech.

The search for an explanation of foetal distress led to a comparison of the placenta/body weight ratio, which was possible in 35 infants (22 mature and 13 premature infants). These results are shown in Table VII.

Thus it appeared that there was a probable significant smallness in the size of the placentae in distressed mature infants when compared with those without distress, but this conclusion

TABLE VIII

The Disposition of Placenta/Body Weight Ratio Amongst 33 Infants (16 Without Haemorrhage: 10 With Anoxic and 7 With Traumatic Bleeding)

Haemorrhages	Premature Infants			Mature Infants		
	Anoxic	Traumatic	None	Anoxic	Traumatic	None
Number of cases with meconium (placenta/body weight ratio) ..	0	0	3 (0·220)	5 (0·191)	3 (0·160)	4 (0·154)
Number of cases without meconium (placenta/body weight ratio) ..	3 (0·353)	2 (0·310)	4 (0·261)	2 (0·181)	2 (0·196)	5 (0·240)

could not be reached in the premature infants; perhaps lack of numbers accounted for this. However, it was not possible to demonstrate any sort of relationship between placental smallness and the incidence of either anoxic or traumatic haemorrhages. This also was probably due to the lack of sufficient cases. The results are analyzed in Table VIII.

Maternal toxaemia had no significant relationship to the incidence of intracranial haemorrhage according to the chi-squared test; for instance, out of 44 cases with haemorrhage 9 mothers had toxaemia of pregnancy, compared with the 57 infants without haemorrhage, amongst whom 10 mothers had toxaemia.

There was a high incidence of ante-partum bleeding in the premature infants with immature brains, 64·7 per cent (11 out of 17 cases) when compared with the premature infants who had mature brains, 25 per cent (3 out of 12 cases) and those who were macerated, 20 per cent (4 out of 20 cases). Since the maternal health was good in most cases (e.g., in 9 out of 11 mothers of infants with mature brains) the material was scrutinized for a fault in the foetus, but it was difficult to arrive at a decision. However, congenital malformations were thought to be unlikely causes since there were several instances of congenital abnormalities where pregnancy had not been complicated by ante-partum loss.

Summary

Details of the necropsy examination and findings in 101 stillborn and neonatal infants are described. Emphasis on the incidence of disease in the nervous system is the prime object of this report and abnormalities were found to occur in the nervous systems of 62 infants (61·3 per cent). Forty-five infants (43·7 per cent) had haemorrhages involving the nervous system. Ten infants (10 per cent) had congenital malformations.

There was a high incidence of breech presentations in infants with intracranial haemorrhages, approximately 10 times the incidence found in all deliveries. Instrumental deliveries had also been frequent.

There was significant smallness of the placenta (placental weight/body weight) between mature infants with foetal distress, assessed by meconium in the liquor, and those without. A similar significance was not found amongst premature babies under similar circumstances.

It was not possible in this series to correlate smallness of placenta with the incidence of anoxic types of haemorrhages into the nervous system.

Maternal toxaemia had no relationship to the incidence of intracranial haemorrhage.

Ante-partum bleeding had been frequent, 64·7 per cent, in premature infants with incomplete external formation of the brain.

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THE MYTH OF TUBAL AND ENDOMETRIAL TRANSPLANTATION

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GYNAECOLOGY claims to its credit various surgical procedures for the treatment of amenorrhoea of traumatic origin. This type of amenorrhoea is a trying sequel to uterine curettage, especially post-partum curettage, and does not yield to hormonal treatment.

Based on the supposition that the endometrium has been destroyed by over-vigorous scraping, which resulted in the partial or total obliteration of the uterine cavity, surgery is intended chiefly to restore the cavity and to replace the lost mucosa by tubal or endometrial tissue.

The first to use a Fallopian tube for this purpose was Paul Strassmann (1935) of Berlin. During the years 1929–1935 he operated on 6 cases of severe dysmenorrhoea without menstrual flow, following curettage of a puerperal uterus, and lasting from nine months to three years. A master of vaginal surgery, he implanted by vaginal route one of the tubes into the artificially enlarged or created uterine cavity. The tube remained with its distal third connected with the mesosalpinx, while the proximal end was attached to the cervical canal by fine catgut sutures. Thus patency of both the obliterated canal and the cavity was re-established.

Menstruation reappeared in weak or normal form 11, 24, 29, 40, 43, 53 days respectively after the operation, and lasted from one to eight days, recurring regularly thereafter. One patient became pregnant and gave birth to a healthy child.

Strassmann could not satisfactorily explain the mechanism of the cure, nor could his son, Erwin O. Strassmann (1956), who recently undertook as an act of filial devotion to bring the method to the attention of the profession.

In spite of the surprising results of the operation, no one tried the method again until recently, when Musset (1957) of Paris and Michalkiewicz (1958) of Poznan, Poland, operated each on two cases by a cervical-abdominal approach; the latter delivered one of his patients a year and a half after the operation by Caesarean section.

Matthaei (1957) of Hamburg simplified the method: he resected 3–4 cm. of the tube, split it longitudinally and implanted it freely into the uterus. The patient promptly regained her menstruation and conceived 9 months later.

A different and seemingly more logical method of treatment was inaugurated in 1929 by the Russian gynaecologist Serdjukoff (1935), who transplanted homeoplastic endometrium. Serdjukoff operated on 3 women by splitting the uterus in the midline and grafting into the remodelled cavity endometrium from a donor of the same blood group. The endometrium, divided in small pieces, was inserted into slits made into the myometrium or sutured to the surface of the wall. The clinical results were excellent and the women, who had been amenorrhoeic for 2, 5, 7 years respectively, menstruated normally.

Nürnberger (1935) followed the method and confirmed its efficacy in one case. He waited for the monthly recurring colicky pains to pass and then transplanted post-menstrual donor mucosa.

Musset (1957) modified the technique by eliminating the affixture of the grafts. The results were equally positive and the patient conceived later on, although post-operative hysterography revealed that the cavity had not been restored sufficiently and a broad adhesion persisted. The patient, 32, amenorrhoeic for 4 years, was at the thirteenth day of her cycle, and the donor, a woman of 37, who had been operated on for haemorrhagic fibroma, was at her tenth day. Six weeks before transplantation a mucous polyp had been removed from her womb by curettage.

A much simpler method of endometrial transplantation, sparing the patients laparotomy and hysterotomy, was published in 1941 by two German scientists, Siebke and Kraatz, independently of each other. Siebke's patient, 32, had been amenorrhoeic for six years, following endouterine cauterization three weeks after delivery. Her sister, barren for many years, with a hypoplastic uterus, volunteered as donor; her menstruation was regular, every four weeks, and the fourteenth day of her cycle was chosen for transplantation. Siebke operated simultaneously on both sisters. First he severed the patient's adhesions by probing and dilating up to Hegar 12, and curetted and dried the uterine cavity.Then he curetted the sister and introduced and emptied the curette laden with endometrial fragments into the patient's womb. This he repeated several times till the entire endometrium was transferred. Hormonal treatment followed.

A specimen taken for biopsy disclosed the donor's endometrium to be underdeveloped and in the proliferative stage. Eleven days later weak menstruation appeared and recurred thereafter, somewhat irregularly, but in normal quantities.

Kraatz used mucosa in its proliferative stage or hyperplastic mucosa, such as can be found in a metrorrhagic or myomatous uterus. The mucosa was cut into 10–15 pieces, immersed in an oily solution of folliculine hormone and finally inserted into the dilated and curetted uterus. The cervix was sutured for eight days in order to prevent the slipping out of the grafts, and hormonal treatment was given. The results were as following: one patient, with tuberculous amenorrhoea, did not respond. Three others, with traumatic amenorrhoea, menstruated promptly and regularly. Moreover, in spite of Kraatz's declared conviction that conception was virtually impossible, one of the three conceived five months after operation and was delivered normally at term. The cavity, upon manual examination, was found normal.

Since then, several authors have published their experiences with the simplified technique, each adding his share to the discussion of the intricate problem. Thus, for example, Wolter (1952), in presenting a case of four years duration—a sequel to post-partum curettage—who menstruated after operation and was pregnant six months later, claims that a graft can under no circumstances heal on a smooth atrophic mucosa and that energetic curettage is indispensable. Besides, the graft must contain all the layers of endometrium including the basalis, which alone possesses the power of restoring the endometrium. Now of what use can fragments be, obtained by curettage?

Heller (1957), who published 4 cases, among them one of tuberculosis, used hypertrophic mucosa gained by curettage and kept in a watery penicillin solution in the thermostat under 37° C. The tuberculous case was a failure; two patients reacted immediately: the fourth, over 35, regained her menstruation only after ten months. Heller rejects Wolter's argument, claiming that there was no evidence that the task of the basalis could not be taken over by the functionalis.

Patat (1943) treated 5 cases of quite different pathogenesis: one case of endocrine dysfunction and climacteric molimina following post-abortum curettage was relieved temporarily for half a year by transplantation and hormonal treatment; one case, a tuberculous endometritis, remained unchanged; a third case, hyperinvolution and amenorrhoea after normal delivery, without traumatization of the mucosa, was operated on after one year and became almost immediately pregnant (*post hoc* or *propter hoc*? G.J.A.). Only two cases were typical traumatic amenorrhoeas and both were cured by the operation.

Grünberger (1957) transplanted a single large strip of endometrium measuring 5×1 cm. and

about 3 mm. thick, removed from a 36-year-old patient, hysterectomized because of a large fibroid. Using the vaginal approach, he pushed back the bladder and the vesico-uterine fold so as to expose the uterus nearly up to the fundus, split cervix and body and inserted and affixed the graft. Post-operatively the patient received antibiotic and hormonal treatment. She conceived two years later.

What makes Grünberger's report so noteworthy is not the fact that he used a single large strip, whereas others divided it into small pieces, but his astonishment over the normal radiological picture seventeen months after the operation, and particularly his explanation as to how the tubes became patent, although no lumen was visible during the operation: "The operation was doubly successful. The mucosa healed and exhibited normal function, as proved by dilatation and curettage. Secondly, the tubes showed a normal passage from the newly formed uterine cavity. This probably can be explained only by the fact that in the course of splitting of the uterus, the intramural portions of the tubes were opened without our noticing it, increased in size, and grew into the transplanted endometrium. This would account for the fact that the uterine cavity gradually assumed its normal triangular shape."

The opening of both tubes by a single midline cut as well as the growing of the tubes into the transplanted endometrium would be miraculous and astonishing, if true.

Tulzer (1958) most recently described a case, in which the obliterated cervical canal had to be split by sharp dissection. No cavity could be found. He inserted a Fehling tube, 6 cm. long, and closed the cut. Ten days thereafter he introduced three strips of proliferative endometrium taken from the uterus of a 43-year-old woman, removed for repeated haemorrhage, and, by a shorter Fehling tube, kept the strips *in situ* for seven days. The patient regained menstruation for two consecutive months and conceived. The pregnancy ended in the seventh month, the premature female baby succumbing two days later.

Solomons (1936) transplanted mucosa from a pregnant myomatous uterus, simultaneously implanting the donor's ovary into the musculus rectus. The patient, aged 31, menstruated regularly thereafter.

Noteworthy, too, is Westman's (1957) experience. He lined the uterine cavity through a small incision with strips of endometrium obtained from a uterus freshly removed because of fibromyoma. Menstruation failed to recur. Two months later he dilated the cervix to admit a Hegar 9 dilator, curetted the cavity and introduced strips of endometrium from a similar source. Menstruation appeared within three weeks and recurred twenty-eight days later. The patient then conceived and gave birth to a premature baby. After a year of normal menstruation, she conceived again, this time carrying pregnancy to term.

After these references, which, of course, are far from being complete, the question arises as to the mechanism by which normal uterine function has been re-established. Even Strassmann does not claim that the implanted tubal mucosa can take over the function of endometrium, nor do all the partisans of endometrial transplantation believe in the healing and functioning of the transplants. These workers have offered various explanations of the mode of action: the transplanted mucosa stimulates the atrophic endometrium; the action is non-specific, comparable to the growth energy of embryonic tissue; it is not the transplant that is effective, but the restoration of the uterine cavity and the removal of inner pressure; the new menstruation comes from original endometrial glands which were embedded and choked in scar tissue and were thus prevented from growing and functioning, etc.

Patat (1943) performed a rather convincing experiment: with the consent of a patient destined for hysterectomy because of intractable menorrhagia and secondary anaemia, he transplanted into her uterus endometrium according to Kraatz's technique. Fifteen days later he removed the somewhat enlarged uterus by the vaginal route. On examination, the flat and homogenous interior was found lined with thin endometrium, with no trace of the transplanted fragments. Beneath the closed external os, there was a clot of blood containing serous detritus, but no cells—the decomposed remnants of the transplant.

In view of the above, what, then, constitutes the *modus operandi*?

To solve the riddle we should like to examine the common denominators of all the cases described:

(1) The traumatic origin. Amenorrhoea started in healthy, fertile and normally menstruating women, following curettage, mostly post-partum, sometimes post-abortum.

(2) Functioning of the ovaries remained normal, as suggested by pelvic discomfort and other menstrual molimina at the time of expected menstruation and proved by vaginal smears or by the basal temperature chart in the more recent presentations. Administration of hormones was, as could be expected, ineffective.

(3) Stricture or obliteration of the cervical canal in the vicinity of the internal os. Strassmann (1935) encountered cervical blockage in one case at 1 cm., in two cases at 2 cm., in the fourth case at 3 cm., and in the fifth case—impossibility of probing. Concerning the latter he noted: "Even the finest surgical probe could not be passed through the internal os." Nürnberger (1935) found blockage at 1 cm. Grünberger (1957) found a medial septum just behind the external os; it was difficult to probe more than 3 cm. to the right or left into the cervical canal. Most authors mention the cervical atresia casually, not knowing that it constitutes the main aetiological factor.

(4) Accumulation of blood behind the cervical block was never encountered, whether the cavity was damaged or not.

(5) In a good number of the cases the uterine cavity was diminished and deformed by adhesions, additional and similar to those in the cervical canal. In some instances the adhesions were so stout that it was difficult to identify the cavity, and a small hollow was all that remained of it. The terms "total atresia" or "complete obliteration" used by most of the authors do not—it seems to us—suit the real findings. In total atresia there must be a complete destruction of the endometrium. But even Strassmann, who speaks of total atresia, found in the majority of his cases some crumbs of tissue, which were microscopically identified as endometrium. Grünberger, on the other hand, noted a small hollow at about the middle of the corpus, but did not succeed in scraping off any tissue whatsoever. The same happened to Kraatz (1941), Wolter (1952) and others, who found a rather normal cavity but no tissue for biopsy.

(6) After breaking down the adhesions, menstrual bleeding returned promptly, if not postponed by overzealous hormonal treatment.

All these common characteristics are exactly the elements of a condition described in 1948 under the name "amenorrhoea traumatica (atretica)" (Asherman, 1948) and supplemented two years later by the description of the so-called "traumatic intra-uterine adhesions" (Asherman, 1950). In both instances the changes are similar, but, whereas in traumatic amenorrhoea the cervical canal and, in particular, the region of the internal os are affected, the intra-uterine adhesions affect the walls of the uterine body proper.

Both conditions are fairly frequent. We have collected in less than ten years over 100 cases of traumatic amenorrhoea and over 250 cases of corporeal adhesions. Communications from other countries, especially France, South America and Scandinavia, confirm this relative frequency. French scientists consider both conditions as one entity, entitling it "syndrome d'Asherman". This consideration is justified by the fact that the adhesions quite often affect both parts of the uterus, cervix and body alike. At the congress of the *Fédération des Sociétés de Gynécologie et Obstétrique de Langue Française* (Marseilles, 1957), a single group (Dalsace, Musset and Netter, 1957) presented 50 carefully studied cases, selected from a much greater material, observed since 1952.

Treatment is surgical, not hormonal. Following manual examination of the size and position of the uterus, the cervix is gripped and an attempt made to pass a sound into the uterus. If resistance is met, the attempt is renewed with narrower surgical sounds which have been bent like the uterine sound. If one of these sounds succeeds in passing the obstacle, the cervical passage is gradually dilated, dilatation ceasing when difficulty is met (usually Hegar 7–8). This marks the end of intervention, and menstruation will ensue at the proper time, namely, four weeks

after the last menstrual pains or at the end of the second phase of the basal body temperature curve. Necessary as gentleness and care are in this measure, the use of a certain amount of force is inevitable. However, an excessive use of force can lead to perforation of the tissues. In certain rare cases the splitting of the obliterated zone or sounding from above may be necessary.

The result of freeing the passage is striking: the endometrium, which was in a state of atrophic quiescence and, therefore, could not be scraped off, or which was scanty with an unusual pattern (alongside of areas of well-developed cyclical phenomena, areas with inadequate secretion and others with scar-tissue changes and closed inactive glands) becomes normal in quality and quantity. Menstruation returns concurrently with the end of the biphasic basal temperature curve or four weeks after the last dysmenorrhoic pains, and recurs thereafter regularly and painlessly. In many instances fertility is restored.

The moot question of pathogeny was discussed in detail at the congress in Marseilles by Netter (1957) and Asherman (1957). The concept, in short, is as follows:

The cervical blockage throws the delicate neuro-endocrine mechanism out of balance. Depressive reflexes are relayed from the diencephalon to the uterus, impairing the response of the endometrium to the hormonal impulses. Removal of the blockage immediately restores autonomic and endocrine functioning. The process is identical with the one sometimes begun with a vesico-vaginal fistula: cessation of menstruation which vanishes rapidly after surgical repair of the fistula.

Coming back to the cases treated by tubal or endometrial transplantation, there can be no doubt that they were typical of "amenorrhoea traumatica", except for the three cases of tuberculosis (Kraatz, 1941; Patat, 1943; Heller, 1957) and the one of hyperinvolution (Patat, 1943) which, of course, did not respond to the treatment. It was, therefore, the recanalization of the uterus, especially the cervix, rather than the transplantation *per se*, which brought about the astonishing therapeutic effects. Hence, it did not matter whether one used tubal or endometrial transplants; the whole tube or part of it; a single large strip of endometrium or many small pieces; the entire thickness or the superficial layer alone; whether the grafts were affixed or left loose; whether the surface of the cavity was denuded by scraping or left intact; whether post-menstrual or inter-menstrual, normal, hypo- or hyper-plastic mucosa or decidua were used; whether one closed the outlet by sutures or left the grafts free; whether post-operative hormonal treatment was administered or not—the results were always the same.

If further proof be needed that the cervical factor is the decisive one, proof is given unwittingly by Westman: the abdominal transplantation was a failure whereas the vaginal transcervical grafting was a complete success. The conclusion is clear and decisive: *traumatic amenorrhoea is cured by restoring cervical patency*; transplantation of any material whatsoever is unnecessary and superfluous. It was a myth—a well-meant one—but a myth all the same.

Summary

Amenorrhoea of traumatic origin does not respond to hormonal treatment, but promptly yields to surgery. During the last thirty years various methods have been tried, all with one goal in view—restoring the partially or totally obliterated cavity and replacing the lost mucosa by tubal or endometrial tissue. The excellent therapeutic results—reappearance of menstruation and restoration of fertility—seemed to justify the approach, and new modifications are still being published.

The transplants used were: the whole tube or part of it; a single large strip of endometrium or many small pieces; the entire thickness or the superficial layer alone; post-menstrual or inter-menstrual, normal, hypo- or hyper-plastic mucosa or decidua. The grafts were affixed or left loose; the surface of the cavity denuded by scraping or left intact; the outlet of the uterus closed by sutures or left open; post-operative hormonal treatment administered or not. The results were always the same.

Critical evaluation shows that all the successfully treated cases belong to the clinical entity described and entitled by us as "amenorrhoea

traumatica", its treatment being: restoration of cervical patency by simple probing and dilatation. This suffices to restore menstruation and fertility. Transplantation of any material whatever is, therefore, of no value and superfluous.

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SURGICAL INDUCTION OF LABOUR IN THE MANAGEMENT OF CONTRACTED PELVIS

BY

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THE purpose of this paper is to give the management of contracted pelvis by surgical induction and the results obtained in a large maternity service. The safety of surgical induction *per se* has been demonstrated in the papers by Gibson (1952) and Tennent and Black (1954).

Premature induction of labour for contracted pelvis is an early method of treatment used in the pre-Caesarean section era when in many cases it held out the only possibility of obtaining a living child. The method had fallen into disrepute due to the greater danger of prematurity to the child, and of sepsis to the mother, in comparison with the relative safety of Caesarean section. There have, however, been some consistent advocates of this procedure such as Drew Smythe (1950) though Johnstone (1955) stated that the Obstetric Congress of 1929 heard "the swan song of that most essentially British of Obstetric procedures the induction of premature labour for contracted pelvis".

Induction of labour for contracted pelvis was commenced with caution in 1950 in the maternity units of the County of Lanark at the Maternity Hospital, Bellshill, and the William Smellie Memorial Hospital, Lanark. In the first year 30 per cent of all cases of contracted pelvis were induced but, as our fears were allayed, we became more confident and in the fifth year of the survey 77 per cent of all cases were induced. During the 5-year period 618 cases of contracted pelvis were delivered and of these 337 were treated by surgical induction and 281 were allowed to go into labour normally or were treated by elective Caesarean section. The figure of 281 includes a small proportion of unbooked cases admitted in labour.

MANAGEMENT

At the thirty-eighth week of pregnancy all cases of contracted pelvis or suspected contracted pelvis were referred from the antenatal clinics to the hospital for assessment under anaesthesia. Where possible radiological pelvimetry was carried out before this date and the plates and measurements were available at the time of assessment. Since the paper by Stewart *et al.* (1956) on the danger of leukaemia in childhood due to antenatal radiology, this procedure is now postponed till after delivery. Practically all cases were examined clinically and assessed by the writer personally. Under intravenous Pentothal anaesthesia, the type of pelvis, degree of contraction and the presence or absence of disproportion were noted.

The membranes were ruptured irrespective of the condition of the cervix provided the following criteria were satisfied, namely—there was no obvious disproportion or only a minor degree of disproportion; the child was considered to be of a reasonable size; the vertex was presenting or external version was successful in a breech presentation; the patient was not an elderly primigravida; fertility was satisfactory and Caesarean section had not been performed on more than one occasion previously. The forewaters were ruptured though at the beginning of this survey hindwater rupture was the usual procedure.

All cases of contracted pelvis delivered during the period 1950–1954 are included and those induced for any indication whatsoever are included in the induced group.

Maternal Mortality

In the 337 cases surgically induced there was no maternal death.

In the 281 other cases 2 deaths occurred—one, a case delivered by forceps and who had a urinary infection treated by Sulphonamides, was discharged on the sixteenth day and died of a pulmonary embolism four hours after leaving the hospital. The second case delivered by Caesarean section under spinal anaesthesia, after a labour lasting twenty-three hours, had post-operative collapse and died nineteen hours after operation. The blood pressure could not be maintained at a satisfactory level despite adequate blood replacement. This death occurred in 1951 and it is possible that modern treatment with Hydrocortisone could have saved this patient.

Maternal Morbidity

There was no case of serious infection in either group. Notifiable pyrexia was noted in 11 cases in the induced group and in 19 cases in the other group. Mild pyrexia was present in 29 cases in the induced group and in 35 cases in the non-induced group. The higher morbidity in the non-induced group is largely accounted for by the greater number of cases treated by Caesarean section.

Foetal Results

In the 337 cases induced, 8 babies were stillborn and 6 died, a total loss of 14 giving an uncorrected foetal mortality of 4·2 per cent. Among these 14 babies, there were 2 cases of gross foetal abnormality, 2 cases of hydrops foetalis and one case of asphyxia associated with accidental haemorrhage. If these 5 cases are excluded the corrected foetal loss is 9 or 2·7 per cent. In addition 2 cases included were induced on account of severe pre-eclampsia, one at thirty-seven weeks and one at forty+ weeks.

In the 281 cases not induced 9 babies were stillborn and 3 died, a total loss of 12 giving an uncorrected foetal mortality of 4·3 per cent. Among these babies there were two cases of intra-uterine death before the onset of labour, one case of foetal abnormality and one case of hydrops foetalis. If these 4 cases are excluded the corrected foetal loss is 8 or 2·9 per cent.

Size of the Baby

The main objection to the method, from the foetal aspect, is the risk of producing small babies which will not survive. In the induced group 38 babies, i.e., 11·3 per cent weighed under 5½ pounds, of which 4 were lost. Of these 4, one case was induced for accidental haemorrhage, there being no foetal heart sounds at the time of induction, and one was induced at 37 weeks for severe pre-eclampsia. This child weighed 4 pounds 5 ounces and subsequently died. Two hundred and sixty-three babies or 78 per cent weighed 5½ pounds to under 8 pounds. Thirty-six babies or 11 per cent weighed 8 pounds or more.

In the non-induced group 27 babies or 9·6 per cent weighed under 5½ pounds and 5 were lost. One hundred and eighty-four or 65 per cent weighed between 5½ pounds and under 8 pounds. Seventy-three or 25·9 per cent weighed 8 pounds or more. There were 3 sets of twins in this group giving a total of 284 babies.

It will be noted that the percentage of premature babies in the induced group is only slightly higher than in the non-induced group and, of the 337 induced babies, loss by prematurity due to the management of contracted pelvis could only be attributed in 2 cases. However, it is seen that only 11·3 per cent of the induced group were 8 pounds or over whereas there were 25·9 per cent in the other group.

The assessment of the size of the baby in the early years caused some concern as the size of the head was used for this purpose. As shown by Hastings Ince (1939) the weight of the baby cannot be assessed by the size of the head. He showed that the average size of head for a 7 pound baby could also be got in babies ranging from 5 pounds to 9·2 pounds. The size of the baby is now roughly assessed by the length, breadth and general impression of the bulk of the uterus excluding cases of hydramnios and this appears to give a much more reliable estimate.

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Type of Pelvis

The type of pelvis was classified as follows: flat 340, sacral deformity 162, contracted outlet 81, asymmetrical 13, lateral contraction 9, generally contracted 12 and spondylolisthesis 1. The pelvis was classified according to type on clinical examination plus radiological pelvimetry and study of the plates where pelvimetry had been possible. Pelvimetry was carried out in 241 of the induced cases and in 181 of the non-induced cases. The principal type was a flat pelvis 4 inches being taken as the lower limit of normal for the conjugata vera at the brim. However, in many of these cases there was also some straightening of the sacrum. Where the true conjugate at the brim was 4 inches or over, but the sacrum was straight reducing the conjugate of the cavity below $4\frac{1}{2}$ inches, then the case was classified as one of sacral deformity. In this group of sacral deformity the brim was usually just within normal limits and any straightening of the sacrum produced a reduction in the cavity. No attempt has been made to classify exactly the degree of contracted pelvis but the majority were of minor degree.

In 456 cases the height of the patient was recorded. Five feet two inches seemed to be a critical height as 395 patients were 5 feet 2 inches or less and only 61 were over 5 feet 2 inches.

Caesarean Section

Thirty-eight or 11·3 per cent of the 337 induced cases required Caesarean section for the following indications: disordered uterine action 17, foetal distress 12, failed induction 4, failed trial of labour 3 and malpresentation and ante-partum haemorrhage 2.

One hundred and fifty-six of the non-induced cases were treated by Caesarean section for the following indications: elective 98, failed trial 22, foetal distress 21, disordered uterine action 8, malpresentation and ante-partum haemorrhage 6 and severe pre-eclampsia 1. The elective group were so chosen on account of 54 with a previous Caesarean section and the remainder on account of disproportion, bad obstetric history and elderly primigravidity.

In the induced group 36 had a previous Caesarean section and of these 25 were delivered vaginally. In the non-induced group 62 had a previous Caesarean section, 4 were delivered vaginally and 58 by Caesarean section of which 4 had a trial of labour.

If the two groups are compared, after eliminating the elective sections from the non-induced group, 11·3 per cent of the induced group required Caesarean section as against 31·1 per cent of the non-induced group who were allowed to go into labour.

Discussion

The main object of this series has been to assess the safety for mother and child of surgical induction of labour as a management of contracted pelvis, and a secondary object was to see if the method reduced the number of Caesarean sections performed for contracted pelvis. It is felt that the first of these objectives has been achieved and that surgical induction of labour gives results comparable to other types of management.

Without a parallel series it is difficult to say that the method has reduced the number of Caesarean sections but the overall section rate of 31·4 per cent does suggest some reduction.

It is now proposed to collect a similar series without induction and thus obtain a section rate for comparison.

The severity of contracted pelvis is gradually becoming less, presumably due to better social conditions and it is feasible that in time the condition may almost disappear. However, disproportion due to a large baby poses a similar problem. As there is no prospect of this condition becoming less frequent, premature induction could be used more widely with a view to reducing dystocia.

Summary

A series of 618 cases of contracted pelvis has been reviewed with special reference to management by surgical induction of labour. Treatment by surgical induction of labour has been shown to be no more dangerous for mother or child than awaiting the spontaneous onset of labour. It is suggested that this method merits a wider trial.

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AN UNUSUAL GONADAL TUMOUR (GONADOBLASTOMA) IN A MALE PSEUDOHERMAPHRODITE WITH TESTICULAR DYSGENESIS

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INTRODUCTION

THE purpose of this communication is to describe a case of an unusual tumour that developed the dysgenetic testis of a male pseudohermaphrodite who had been examined in the Endocrine Out-Patient Department because of primary amenorrhoea. The tumour was composed chiefly of germ cells and was originally classified as an atypical seminoma. More thorough histological examination, however, revealed the additional presence of Leydig cells as well as cells that had an appearance consistent with either Sertoli cells or granulosa cells. Tumours containing combinations of these cells recapitulate the structure of the foetal gonad and have been named by Scully (1953)—gonadoblastoma.

Since the original description only one other tumour has been reported as belonging to this category (Santesson and Marrubini, 1957). According to Scully, however, the gonadoblastoma is probably not as uncommon as the rarity of recorded cases suggests. It is very likely that some of these tumours have been wrongly identified as pure dysgerminomas. The tumours reported by Ber (1949), Plate (1953) and Blocksma (1955) could, in Scully's opinion, be gonadoblastomas, but the description and illustrations of the microscopic findings in this case are not sufficiently detailed to permit a definitive diagnosis.

Since the pure dysgerminoma contains no cells that are capable of hormone production there are two explanations when virilism is associated with a tumour of apparent germ cell origin.

(1) Adjacent to the germ cell tumour there may be an overgrowth of hilus (Leydig) cells resulting in androgen production and masculinization (Gough, 1938; Usizima, 1956).

(2) Growth of Leydig cells may occur within the tumour proper. This was observed in one of Scully's cases as well as in the case to be reported below.

CASE REPORT

Patient C.A. (No. 5594), 19 years of age, was referred to the Endocrine Out-Patient Department because of failure to develop female secondary sexual characteristics, primary amenorrhoea and shortness of stature. At 12 years of age pubic hair began to develop. Shortly thereafter axillary hair appeared and at this time an enlarged clitoris and deepening of the voice were observed. Psycho-sexual orientation was definitely female.

Biotypological examination. The body contour was that of a male. Weight, 41·7 kg.; height, 146 cm.; span of arms, 149 cm.; circumference of chest, 76 cm.; bitrochanteric measurements, 26 cm.; bihumeral measurements, 35 cm. A

morphogram (Decourt and Doumic, 1950) revealed a curve similar to that of the male morphotype. The skin was pale and oily, axillary hair was absent and there was a male distribution on the forehead. The breasts were adolescent with palpable breast tissue and the nipples were widely separated on the broad chest (Fig. 1).

Gynaecological examination. The pubic hair showed an adult female distribution. It spread to the medial surfaces of the thighs but not up to the linea alba. The clitoris was enlarged, measuring 4 cm. × 1·5 cm. and was covered by a large preputial fold that contained smegma (Fig. 2). The labia minora appeared normal. The labia majora were hypertrophied and were covered by wrinkled and rugged skin of scrotal appearance. A raphe was distinctly visible in the perineal region. The vagina was narrow and admitted only one finger; its walls were smooth. The cervix was as thick as a pencil. The fundus of the uterus was palpable and was smaller than a cherry. The axis of the fundus was a prolongation of the axis of the cervix, which is typical for the foetal uterus. The left gonad was not palpable. The right gonad was enlarged to the size of a walnut and was round and very compact.

Pertinent laboratory studies. The skeletal age was approximately normal. The chromosomal sex determined by skin biopsy and vaginal and buccal smears was male. 17-Ketosteroid urinary assay levels varied from 5·0 to 7·3 mg./day. The basic metabolic rate was plus 9. Gonadotrophin assay levels were above 100 but less than 200 mouse units. Vaginal smears showed non-cyclical cytological curves, characterized by the absence of eosinophilic cornified cells and the presence in varying proportions of basophilic non-keratinized cells and intermediate cells with vesicular nuclei.

On the basis of these assays and in view of the ambisexual stigmata a diagnosis of a form of intersexuality intermediate between gonadal dysgenesis and classical male pseudohermaphroditism (or Turner's syndrome with masculinization) was made. To establish a final diagnosis and to explore the possibility of a tumour of the right gonad, laparotomy was performed (by Dr. Pyrzakowski of the Department of Surgery, Municipal Hospital No. 4).

The findings at operation were as follows: the uterus and Fallopian tubes were pre-adolescent. On the posterior surface of the left broad ligament in the location normally occupied by the ovary a typical dysgenetic gonad was found in the form of a whitish ridge, that measured about 3·5 cm. in length and 4 mm. in diameter (Fig. 3). On the right broad ligament also in the location normally occupied by the ovary a tumour measuring 5·5 cm. × 4·5 cm. × 3·5 cm. was found. Its surface was smooth and glistening. On section the neoplastic tissue was firm and lobulated. Miliary calcific foci were palpable on the sectioned surfaces (Fig. 4).

The left gonad, the tumour of the right gonad and both Fallopian tubes were removed.

Microscopic examination. The histologic features of the left rudimentary gonad were as follows: the cortical part resembled normal spindle-celled ovarian stroma arranged in whorling fashion. In this cortical stroma germinal follicles were absent.

In the medullary region tubules lined with immature Sertoli cells were seen. Typical Leydig cells were lacking. However, there were rare cells that may have been Leydig cells. These were of variable size being chiefly small and fusiform with finely granulated eosinophilic cytoplasm (Fig. 5). A few tubules showed extensive hyaline degeneration.

In the hilar region numerous tubules lined by a single layer of cuboidal cells were present. These appeared to be of mesonephric origin. On the left side an immature Fallopian tube was present. In addition in the adjacent mesosalpinx ductuli efferentes of epididymis and vas deferens were found.

The histologic features of the tumour of the right gonad were as follows: the capsule was made up of fibrous tissue resembling ovarian stroma. The neoplastic tissue was lobulated (Fig. 6) and was composed of cells arranged in round or oval nests with scanty lymphoid stroma. Throughout the entire tumour germ-cell elements were mixed with cells of Sertoli or granulosa type (Fig. 7). The distinctive patterns of these cells, as described by Scully, were recognized in various areas, mainly in the regions close to the capsule (Fig. 6). The Sertoli or granulosa cells were arranged in coronal fashion

about germ-cells in single file, usually along the periphery of the nests and in folliculoid arrangement surrounding eosinophilic bodies (Fig. 7).

Structures resembling the polyovular follicles of the foetal ovary and the tubules of the foetal testis were also found (Fig. 8). (Note the close similarity to Figure 11 in Scully's (1953) paper.) In other sections the tumour cells were arranged in oval and tubular nests resembling seminiferous tubules (Fig. 9). This pattern suggests the tendency of the neoplastic cells to differentiate along testicular lines. The tubular walls were composed of 2–3 concentrically arranged layers of oblong, thin connective tissue cells with flattened nuclei. The epithelium of the tubules consisted of a few rows of Sertoli cells and germ-cells (large cells with clear cytoplasm).

In some areas a picture more or less typical of the "pure" dysgerminoma was present (Fig. 11). Other regions showed small tubules lined by oblong Sertoli cells recalling the oestrogenic "tubular granulosa-cell tumour" (or androblastoma tubulare lipoides of Teilum, 1949). Elsewhere, a proliferation of Leydig cells created a picture similar to that of a pure interstitial cell adenoma (Fig. 12). An arrhenoblastoma-like pattern also was found. Large areas of the tumour were characterized by a confusing admixture of the various cell types in malignant fashion. Finally, in still other sections the stroma contained calcific foci separated by large groups of Leydig cells (Fig. 13). The above histological picture is in accordance with the morphologic criteria for the "gonadoblastoma" proposed by Scully, who confirmed the diagnosis on the basis of photomicrographs and slides of the present case, which were submitted to him.

The post-operative course was uneventful. Eight days after the operation menstrual bleeding from the uterus appeared for the first time in the patient's life. This bleeding was analogous to the oestrogen-withdrawal bleeding that appears in patients after ovariectomy. Since the first episode of bleeding the following hormones have been administered: thyroid tablets containing 0·2 per cent iodine, once a day; stilboestrol, 1 mg. daily; oestradiol ampoules containing 50,000 units (5 mg.) in 1 ml. administered intramuscularly, five every second day between the 10th and 20th day of this regimen and folic acid, 30 mg. a day. Between the 20th and 21st days of this regimen intramuscular injections of 30 mg. of progesterone were given. Eight days after completion of the regimen menstruation appeared for the second time. A considerable development of the breasts and vagina has occurred after six months of treatment.

Discussion

This case may be diagnosed as testicular dysgenesis manifested clinically by short stature (characteristic of Turner's syndrome), hypoplastic breasts, retarded sexual development (primary amenorrhoea, infantile vagina and uterus), a high gonadotrophin level and a male sex chromatin pattern. On the other hand definite signs of hermaphroditism were present. The patient's psycho-sexual orientation was definitely female, she felt like a woman and desired to be a woman. At the age of 13 her voice deepened. Inspection of the external sex organs revealed a penile clitoris and labia covered by wrinkled skin of scrotal appearance (Fig. 2). A raphe was distinctly visible in the perineal region. At laparotomy the tubes and uterus appeared small but were otherwise normal and the gonads had the typical location of ovaries on the posterior aspects of the broad ligaments. The right gonad was partly replaced by tumour, the left gonad showed the typical gross appearance of gonadal dysgenesis (Figs. 3 and 4).

Microscopic examination of the left gonad revealed dysgenetic seminiferous tubules (Fig. 5), according to Nelson's definition (1958). High urinary gonadotrophin excretion provided clinical evidence of gonadal hyperfunction. According to these findings the case might be classified either as: (1) male pseudo-hermaphroditism with testicular dysgenesis, or (2) male pseudohermaphroditism with testicular feminization. The latter interpretation was suggested by Nelson, who examined the photographs of the patient and the photomicrographs of the left dysgenetic gonad. However, the gonadal abnormalities in this case were more marked both from structural and functional standpoints than those associated with typical testicular feminization as described by other writers (Morris, 1953; Greenblatt, 1956; Teter, Bulska and Ruszkowski, 1959). It

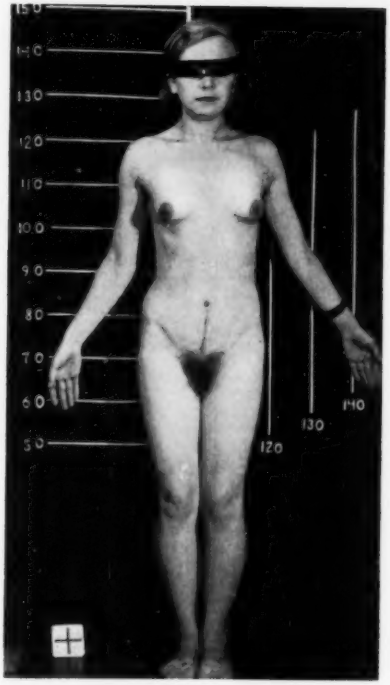

FIG. 1

Patient C.A. Diagnosis: Intersexuality intermediate between gonadal dysgenesis and male pseudo-hermaphroditism with testicular feminization.

FIG. 2

The enlarged clitoris and the labia of scrotal appearance.

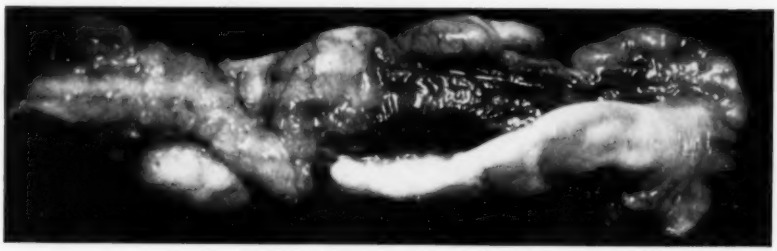

FIG. 3

The left infantile Fallopian tube and dysgenetic gonad.

FIG. 4

Tumour of the right gonad (gonadoblastoma). The cut surface is coarsely lobulated and shows scattered yellow calcific flecks.

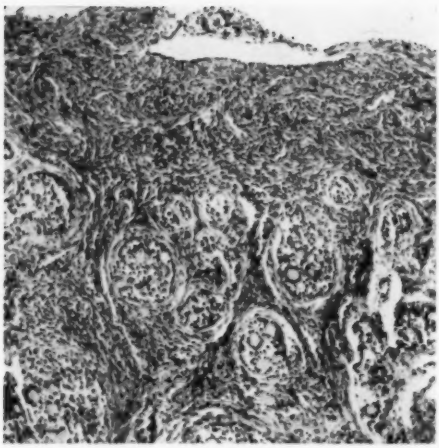

FIG. 5

The rudimentary testis on the left side. Low power photomicrograph illustrating the cortical part resembling ovarian stroma. In the medullary region are dysgenetic seminiferous tubules.

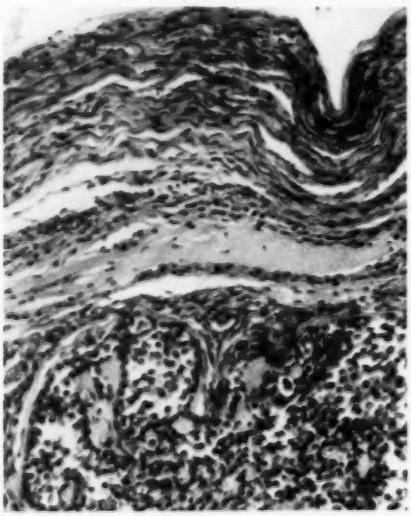

FIG. 6

The capsule of the tumour is made up of fibrous tissue resembling ovarian stroma (top). The neoplastic tissue is lobulated (bottom), and composed of germ cells and Sertoli cells.

FIG. 7

The most characteristic structures of the tumour closely resembling "the gonadoblastoma" described by Scully (1953). Small cells with oval and bent nuclei arranged in "coronal" fashion about germinal cells. Other small cells (Sertoli cells) are in peripheral single file, along the base of the pseudo-tubules.

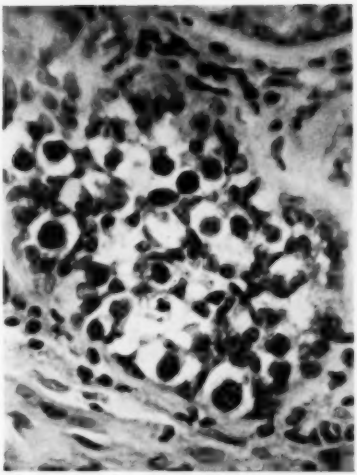

FIG. 8

Small area with structures resembling polyovular follicles of the foetal ovary or the embryonic testis in the neutral stage before tubular differentiation.

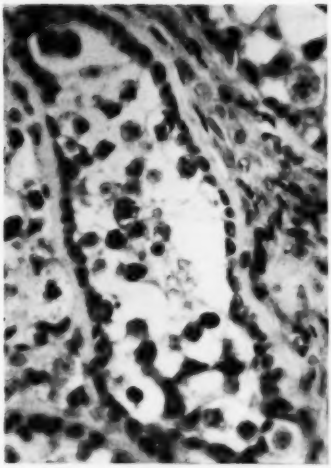

FIG. 9

A nest of Sertoli-type cells and germ cells in an arrangement resembling seminiferous tubules. This picture suggests the tendency to differentiation along testicular lines. ×280.

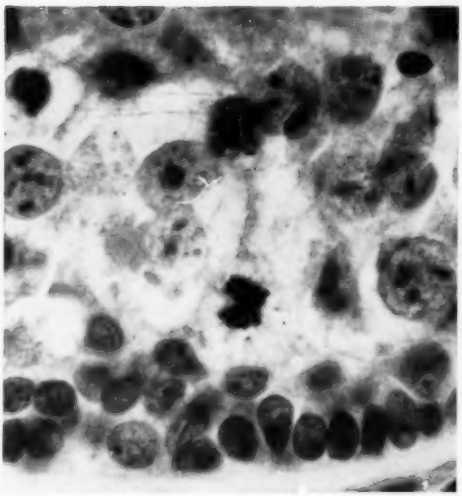

FIG. 10

The Sertoli cells (bottom) and germinal cells. Note nuclear grooving characteristic of Sertoli cells.

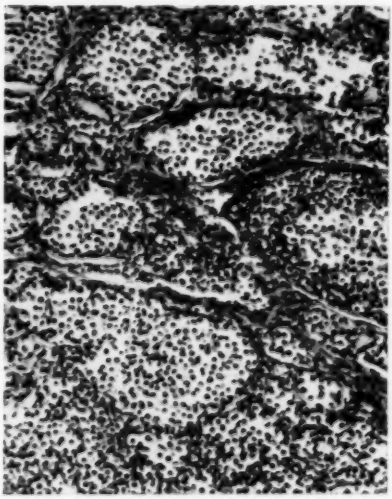

FIG. 11

Detail from one of the tumour nodules showing the dominating germinal cells in large foci, surrounded by a lymphoid stroma.

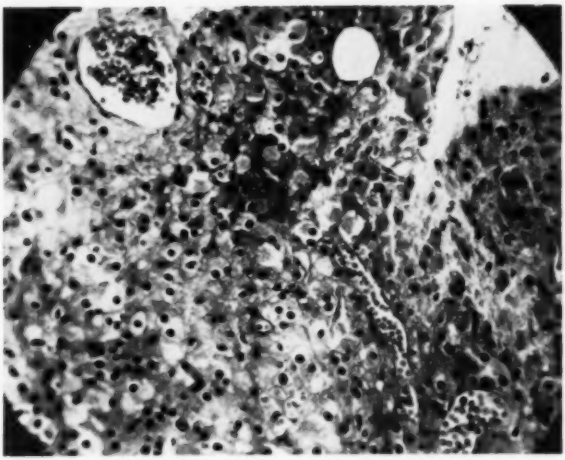

FIG. 12

An area composed of cells of Leydig-theca-lutein type, similar to "pure" interstitial cell tumour.

FIG. 13

The calcified concretions surrounded by hyalinized connective tissue. In periphery three small collections of Leydig cells.

seems very likely that in this case the testes had been inhibited to a severe degree in their foetal development. The Müllerian duct derivatives (uterus, tubes) developed but the Wolffian duct derivatives failed to form, indicating the absence of any testicular factor during the time of duct differentiation.

The gonads apparently failed to recover sufficiently to provide good stimulation of the breasts and the female habitus to the degree observed in classic testicular feminization. Some weak oestrogenic stimulation resulting in endometrial proliferation must have existed as uterine bleeding of withdrawal type (the first in the patient's life) followed surgical removal of the dysgenetic and neoplastic gonads. Possibly Sertoli cells were the source of such oestrogens. These cells were present in the dysgenetic seminiferous tubules of the left gonad but were better developed and more numerous in the right gonad where they formed an integral part of the tumour. The androgenic manifestations (deep voice, acne, seborrhoea, enlarged phallus-like clitoris) can be attributed to secretory activity on the part of Leydig cells. In the left gonad typical and well-formed Leydig cells were lacking but they were present in large quantities within the neoplastic gonad where they were arranged in several patterns: (1) in small groups in the interstitial tissue surrounding the pseudo-tubular structures formed by neoplastic cells of germ and Sertoli type (Fig. 9), (2) in larger calcified concretions in the surrounding hyalinized connective tissue (Fig. 13), (3) in diffuse masses resembling a pure interstitial cell tumour (Fig. 12). In the latter regions the Leydig cells had a morphological appearance similar to those of theca-lutein or adrenal-like cells.

Tumours with the above microscopic structure are rare, having been previously described only by Scully (1953) and by Santesson and Marrubini (1957).

The two tumours of Scully developed in patients with primary amenorrhoea and disturbed sex development. No gonadal tissue uninvolved by tumour was identified. In view of these cases and the present case it seemed highly probable that these tumours characteristically arise in patients with the syndrome of gonadal dysgenesis.

Summary and Conclusions

(1) A case of defective sex development in a patient registered as a female, with female psycho-sexual orientation, complaining of primary amenorrhoea and short stature has been presented. Clinical examination revealed: hypoplastic breasts, pubic hair of female distribution, a penile clitoris and labia with a scrotal appearance (Turner's syndrome with masculinization). Laboratory findings included an elevated gonadotrophin titre in the urine and a male sex-chromatin pattern. Male pseudo-hermaphroditism with testicular dysgenesis was consequently diagnosed.

(2) Exploratory laparotomy revealed the presence of Müllerian derivatives: fimbriated Fallopian tubes and an infantile uterus. A dysgenetic gonad in the form of a whitish genital ridge was identified on the left. A tumour the size of a pigeon's egg was located in the right mesosalpinx. Both tubes, the genital ridge and the tumour were removed. Uterine bleeding, the first in the patient's life, appeared on the eighth post-operative day and provided evidence of oestrogenic gonadal activity.

(3) Microscopically the left genital ridge showed single germ cells and immature Sertoli cells in the medullary zone. The cortical zone contained fibrous tissue resembling ovarian stroma. Epididymal tubules were found in the adjacent mesosalpinx close to the left tube.

(4) Microscopic examination of the right gonadal tumour revealed an unusual neoplastic mixture of three types of cells: germ cells, cells resembling Sertoli or granulosa cells, and Leydig cells in arrangement suggesting the structure of foetal gonads particularly the testis. The tumour also bore a resemblance in areas to certain homologous tumours of testis and ovary (interstitial cell tumour, arrhenoblastoma, Sertoli cell and granulosa cell tumours). On the basis of these findings the tumour was classified, according to Scully's term, as gonadoblastoma.

Acknowledgments

I wish to record my thanks to Dr. Warren O. Nelson (New York) for his interest in the diagnosis of this case. I am indebted particularly

to Dr. Robert E. Scully (Boston, Massachusetts) for reading the manuscript, for helpful criticism of the commentary and for his helpful suggestions on different aspects. I have to thank also my clinical colleagues in Warsaw—Dr. Jurewicz and Dr. Tarłowski for help in the diagnostic procedures in this case.

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THE EDINBURGH FLYING SQUAD—A REVIEW 1948–1957*

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THE Flying Squad based on the Simpson Memorial Maternity Pavilion Edinburgh, received its first call on the 4th February, 1948, and thus has been in existence for just over 10 years. Plans were being prepared for the formation of a Squad in 1939, but they could not be proceeded with because of the intervention of the Second World War during which the Staff was not available to provide an Emergency Service.

The main reason for the formation of this service was the realization that a certain number of women lost their lives because they had to be moved to hospital for treatment. This especially applies to patients with retained placenta or post-partum haemorrhage, with incomplete abortion or ante-partum haemorrhage or with any other obstetric condition associated with shock. As will be discussed later, third stage complications account for most of the calls received. In the 10 years prior to the inception of the Edinburgh Squad, 10 patients died from post-partum haemorrhage very soon after admission to the Simpson Pavilion and there must have been other similar patients who were admitted to the other maternity hospitals in the region or who died in their own homes.

The area covered by the Simpson Squad extends roughly from the Forth Estuary to the English border and from the East Coast to a line roughly halving the South of Scotland, an area of approximately 2,400 square miles. This is a very large area and calls are received from as far away as 60 miles.

In Edinburgh, the Flying Squad has consisted, since its inception, of a Registrar or, in some cases, a Consultant Obstetrician, a House Surgeon and a Sister or Staff-Midwife. Whether the staffing of such a Service should be rigid or should be made more flexible is to our minds a question which merits discussion, and changes might be made in the personnel according to the type of case to which the Squad has been summoned. For example, in a case of retained placenta or incomplete abortion when an anaesthetic will be necessary, it would seem reasonable for an anaesthetist to take the place of the House Surgeon. The Newcastle Squad now includes a Consultant Anaesthetist and we would like to return to this question later in this communication.

Transportation is the responsibility of the St. Andrews Ambulance Service and there is always a vehicle and driver standing by at the garage so that we rarely have to wait longer than five minutes for its arrival. An ambulance has, of

* Based on a paper read to the Edinburgh Obstetrical Society, March, 1957.

TABLE I
Flying Squad Calls Per Annum

Year	1948	1949	1950	1951	1952	1953	1954	1955	1956	1957
Number	46	36	39	45	45	38	22	41	49	42

course, the advantage over a private car that the patient can be brought back to hospital, if necessary, without delay.

The Flying Squad can be summoned by any general practitioner or, if he is not present or not readily available, by the midwife in charge of the case. We feel that this latter alternative is very important since, if a practitioner has departed on his rounds, much valuable time may be wasted and the patient's life jeopardized, if the midwife has not the authority to summon the emergency service. We were interested to see in the *British Medical Journal* of 20th April, 1957, that the General Medical Services Committee of the B.M.A. has now approved of permission being granted to the midwife to call the Flying Squad at the same time as she calls the general practitioner.

When a call is received at the hospital it is immediately switched to the Labour Ward where the Senior Sister records the essential details in a book, special care being taken to record the exact location of the patient's house. If any difficulty is likely in quickly finding the house, the Doctor is asked to station a responsible person, such as the husband, at a pre-arranged spot so that the Squad can be guided to its destination. We have occasionally found the police very helpful in acting as guides. Preparations are immediately set in motion for the departure of the Squad and at the same time the Labour Ward Sister contacts the duty registrar so that he can speak to the doctor. We consider this very important, firstly because an accurate history and diagnosis is of great help and, secondly, because it is often possible for the registrar to offer the practitioner advice on treatment which can be carried out while the Squad is on its way. There does seem to be a reluctance to administer intravenous ergometrine if the patient is bleeding heavily in the third stage or even after the placenta is delivered. The administration of morphine and raising the foot of the bed are other points of advice which can be given. If the Squad has some distance to travel then it is of great assistance if an intravenous infusion can be set up. A bottle of Dextran can be kept indefinitely and is an adequate temporary substitute for blood.

We now turn to a review of the 403 cases treated during the past 10 years. Table I shows the number of calls in each year and we see that there has been a considerable variation from 22 in 1954 to 49 in 1956. There seems no adequate explanation for this. It is seen that the yearly average is 40. According to Harvey Evers (1957) there has been a steady increase in the number of calls received in Newcastle and in 1955 the total had reached 146.

Although the majority of patients have been treated in their own homes we have also answered calls to nursing homes and cottage hospitals and the numbers in each category are shown in Table II. We have divided the location of the calls into "Edinburgh" and "distant" and have found that 47 per cent were local and 53 per cent were distant. On a rough estimation we have calculated that in these 10 years the Squad has travelled in the region of 10,300 miles, representing an average of 26 miles per call.

TABLE II
Location of Calls

Own home	294
Nursing home	67
Cottage hospital	42

As is to be expected, while the reasons for calling the Squad have been numerous, the predominant ones are retained placenta and postpartum haemorrhage. In Table III are listed the most important conditions and it is seen that retained placenta accounted for 187 calls and

TABLE III

Reason for Calling Out Squad

Retained placenta	187
Post-partum haemorrhage	133
Abortion	34
Eclampsia	7
Puerperal haemorrhage	8
Ante-partum haemorrhage	7
Traumatic haemorrhage	4
Miscellaneous	23

post-partum haemorrhage 133, representing 79 per cent of the series. This agrees closely with the Newcastle figure of 75 to 80 per cent. The term post-partum haemorrhage has been used here in its true sense and cases of third stage haemorrhage have been listed under retained placenta. The third commonest condition is abortion and these three conditions together account for 88 per cent of all the calls.

Of the 23 miscellaneous calls, there were 3 cases of acute inversion of the uterus and 1 case of a severe haematemesis during the third stage of labour. There were also 4 gynaecological conditions, comprising 1 ectopic pregnancy, 1 haemorrhage from carcinoma of the cervix, 1 haemorrhage from fibroids and 1 haemorrhage following a total hysterectomy. One forceps delivery and 2 breech extractions were performed but we do not consider that delivering patients is a normal function of a Flying Squad. Transfer to hospital can usually be quickly arranged and this is very much more satisfactory as a proper obstetric table, expert anaesthesia and a good light will make the delivery much safer for both mother and child.

In the next part of this paper, the number of cases which we have been able to analyze has fallen by some 50 as only 349 cases have been sufficiently documented for detailed study.

Table IV shows the degree of shock present on arrival of the Squad. The systolic blood pressure level has been used in this classification, a level above 90 mm. mercury being classed as mild, between 90 and 60 as moderate and below 60 as severe. The first and last lines are self-explanatory. As is seen, the largest group is that in which there was no shock present and this is largely accounted for by the number of cases of retained placenta in which there had been little or no associated bleeding. The next largest group is that with moderate shock, that is a systolic blood pressure between 90 and 60 mm. and of these there were 93. Thirty-nine cases were classified as severe shock and it is obviously in this group that deaths would have occurred if all these patients had initially been sent into hospital.

TABLE IV

Degree of Shock on Arrival of Squad

Nil	128
Mild	86
Moderate	93
Severe	39
Dead	3

Three hundred and sixty-five pints of blood were administered in the cases which were documented and, if we exclude the patients with no shock and those dead on arrival, this represents 1·6 pints of blood per patient treated. In the first few years of the existence of the Flying Squad a box of typing sera was included in the equipment and attempts were made to cross-match all the blood administered. However, this method was not very accurate in rather inexperienced hands and in addition was time-consuming. At present, Group O Rh negative blood is carried unless, of course, the patient's group is known, and this eliminates to a high degree any danger of incompatibility. In addition to blood, 12 pints of Dextran, 4 pints of plasma and 2 pints of saline were used.

We now turn to the obstetric treatment carried out in this series and the most important procedures have been summarized in Table V. As would be expected, treatment of retained placenta accounts for most of the operative procedures. We have found remarkably little difficulty in carrying out manual removal of a

TABLE V

Operations Performed by Flying Squad

Manual removal of placenta	121
Expression of placenta from vagina	32
Evacuation of uterus	9
Suture of lacerations	4
Replacement of inverted uterus	2
Salpingectomy	1

placenta even under the most unfavourable conditions. Occasionally there has been very little space for anything but the bed in the room and once or twice the only available light has been from a paraffin lamp. Nevertheless, with a little ingenuity, especially on the part of the nurse, adequate preparations can be made and reasonable asepsis obtained. We would like to record here our indebtedness to the many sisters and staff midwives who have accompanied us on Flying Squad calls. They have played a very big part in the successful running of this service and their help has been invaluable.

We now return to the question of anaesthesia. In 138 cases it was considered necessary to administer a general anaesthetic and the various types which have been used are shown in Table VI. It is only necessary to consider the first two

TABLE VI

Anaesthetic Agent Employed

Chloroform	107
Pentothal	23
Cyclopropane	1
Not stated	7

as the case which received Cyclopropane was dealt with in a cottage hospital.

In our view, anaesthesia is the least perfect and perhaps the most dangerous aspect of a Flying Squad call. However, there have been, to our knowledge, no anaesthetic deaths. The anaesthetic is usually given by the house surgeon, although if the general practitioner wishes to act as anaesthetist we are only too pleased to have his assistance. From the patient's point of view this is probably helpful as she will obviously have more confidence in her own doctor than in a complete stranger. Also it gives the practitioner the feeling that he also is a member of the team, and this we welcome.

The choice of anaesthetic in a patient's home is, of course, strictly limited by such factors as inflammability, equipment available and the experience of the doctor who is to act as anaesthetist. Pentothal is a drug which is easily transported and its administration presents little difficulty but it has fairly marked disadvantages. In the first place, it lowers the blood pressure and this is undesirable if a patient already has some degree of shock. Secondly, in inexperienced hands it has a high death rate compared with other anaesthetics, partly due to the danger of spasm of the vocal cords. An oxygen cylinder is included in our equipment and this is fitted with a Guy-Ross bag which would enable forced breathing to be initiated if required. The third disadvantage is that, when a difficult manual removal of placenta is being performed, complete relaxation of the patient is essential and this cannot be obtained with Pentothal unless the patient is at a dangerously deep level of anaesthesia. In examining the records of the Squad calls we have noted that most of the cases in which Pentothal was used occurred in the earlier years and it seems that our confidence in this drug has gradually waned.

Chloroform too is easily transported and is non-inflammable, and again its administration should present no difficulty. It gives excellent relaxation of the abdominal wall and the uterus, and greatly facilitates any intra-uterine manipulations. This anaesthetic also is not without its dangers as it is quite easy to produce a dangerously deep level of anaesthesia and there is also the possibility that a patient, not properly prepared for operation, may vomit and inhale. However, with our present personnel and equipment, we consider that open chloroform is the best anaesthetic available to us. As mentioned previously, when an anaesthetic is likely to be required, the best solution would be to have a specialist anaesthetist included in the Squad.

As a general rule patients are not brought into hospital after treatment by the Flying Squad but, in some instances, admission to hospital is essential and in others, treatment is facilitated if the patient is transferred. For example, it is essential to bring in cases of eclampsia and ante-partum haemorrhage while, in a case of incomplete abortion, treatment is much easier if the patient is admitted. In all, 62 cases or 15 per cent were transferred to hospital after initial treatment at home. These are summarized in Table VII. As is to be expected abortion heads this list with 21 cases, followed by eclampsia with 8. This latter condition would appear to be an ideal one for treatment by the Flying Squad. One of the fundamental principles is to prevent the patient having

TABLE VII
Cases Transferred to Hospital

Abortion	21
Eclampsia	8
Laceration	4
Ante-partum haemorrhage	4
For observation	9
Miscellaneous	16

further fits and prior to the formation of the Squad it was fairly common to admit patients who had had two or three fits in the ambulance during transportation to hospital.

RESULTS

Out of the 403 cases attended there were 5 deaths, representing 1·2 per cent. Of these, 3 were found to be dead on arrival of the Squad and we wondered if there had been any unnecessary delay either in summoning the Squad or in its arrival. In the first case, 17 miles distant, there was a dense fog which delayed the Squad considerably and the journey took just over an hour. The second case illustrates very well our remarks on the advisability of midwives being allowed to summon the Squad if they cannot at once contact the general practitioner. This patient collapsed 7 hours after delivery. The doctor had just left on his morning round and was not contacted for nearly 90 minutes, by which time the patient was moribund. In the third case there was no delay.

Of the 5 deaths, there were 3 cases of post-partum haemorrhage, 1 case of third stage haemorrhage and 1 acute inversion of the uterus. The case of third stage haemorrhage was dead on arrival as were 2 of the 3 cases of post-partum haemorrhage. The third case followed the delivery of twins and the Flying Squad was in attendance for 12 hours before the patient died. Although she was given 6 pints of blood and 1 pint of plasma her condition gradually deteriorated and she had obviously reached the stage of irreversible shock. In the case of the acute inversion, the uterus was outside the vulva with the placenta still attached. The practitioner removed the placenta and although there was little bleeding the patient rapidly became deeply shocked and died within five minutes of the arrival of the Squad.

In conclusion we would like to make a few general observations. During the 10 years under review we have had comparatively few unnecessary calls. We fully realize how quickly a patient, who has perhaps been given morphine and the foot of her bed raised, may recover although at the time that the call was initiated she may have had a fairly marked degree of shock. We trust that when these circumstances have arisen we have not given the general practitioner the impression that we thought that he had been wasting our time because this is certainly not so. We should, however, mention here one type of case which we do not consider to be an emergency. On several occasions we have been called to see patients, delivered 24 or even 48 hours previously, who perhaps had had a post-partum haemorrhage and who as a consequence had become anaemic. The Flying Squad should not be used as a Blood Transfusion Service. The best way for the practitioner to deal with such patients is to send a specimen of blood to the Blood Transfusion Department where it can be properly cross-matched. We would stress that a Flying Squad is an emergency obstetric service and we would like to summarize the various conditions for which it should be summoned. Firstly, third stage complications. A patient with a retained placenta, even if she has had no bleeding and is perfectly fit should never be sent into hospital as there is no guarantee that she will not bleed profusely during her journey. Third stage or post-partum haemorrhage causing the patient to become shocked is an obvious reason for a call but we feel that the earlier use of intravenous ergometrine could cut down the number of these cases. Ergometrine is a more powerful oxytocic drug than Pituitrin and is much safer. Incomplete abortion associated with shock is the second condition justifying a call for assistance. Thirdly, as previously mentioned, we consider that a patient who has had an eclamptic fit or is in imminent danger of doing so, is a suitable case for treatment by the Flying Squad. Fourthly, if a patient has severe lacerations from which there has been blood loss sufficient to produce shock, the Squad should be called. Again we would

stress the presence of shock because if such a patient is fit to travel it is much more satisfactory to deal with her in hospital. It is unusual for a patient with an initial ante-partum haemorrhage to develop shock but if this should happen then the Flying Squad should be summoned to resuscitate her and transport her to hospital. Occasionally, other indications may arise, and if the practitioner is in doubt as to whether or not to call the Squad, there is always someone on duty in the hospital who will be glad to advise him.

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PROBLEMS IN THE TREATMENT OF THE INCOMPETENT INTERNAL OS

Report of a Case Associated with Twin Pregnancy

BY

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INCOMPETENT internal os is being more commonly recognized as a cause of mid-trimester abortion and premature labour. As operative intervention to correct this condition is attempted more frequently, new problems connected with the management of these cases come to light. Many of the forms of operative treatment have been previously discussed by Lash and Lash (1950), McDonald (1957), Green-Armytage and McClure Browne (1957), Barter *et al.* (1958) and others.

No case of twin pregnancy successfully treated by cervical ligation has so far been reported. The increased uterine size and the relatively early formation of the lower uterine segment associated with multiple pregnancy places a far greater strain on the incompetent sphincter mechanism and the difficulties associated with such a case are naturally accentuated; they shed light on the problems attendant, to a lesser degree, on single pregnancy associated with this condition.

A critical analysis of the management of such a case will, I believe, illustrate the difficulties of successful ligation as well as some of the complications that may arise following the operation.

CASE REPORT

Mrs. E.S., age 27 years, multigravida.

Previous Obstetric History

1954—Premature labour commenced at 28-weeks gestation following rupture of the membranes. She was delivered of an infant of 2 pounds 4 ounces which died after 6 hours.

1956—Premature labour commenced at 28-weeks gestation. The membranes ruptured on admission to hospital and she was delivered of an infant of 2 pounds 1¾ ounces which subsequently survived.

1957—During this pregnancy she was examined vaginally at weekly intervals from the 18th week onwards. The internal os was found to be one finger's breadth dilated at 27-weeks gestation and bulging of the forewaters was present. Cervical ligation was performed by the modified Shirodkar technique (as described later). The suture was removed at 38-weeks gestation and low artificial rupture of the membranes was performed. After a 3½-hour labour, she was confined of a living infant of 5 pounds 12 ounces which survived.

Previous Health

She gave no history of previous abortion nor of operative dilatation of the cervix. In 1955, diathermy conization of the cervix was performed for chronic cervicitis with laceration.

Present Pregnancy

She was first seen on 30th September, 1958, with a history of 7-weeks amenorrhoea. Vaginal examination confirmed the presence of a uterine pregnancy. Multiple pregnancy was first suspected at 14-weeks gestation because of a uterine size equivalent to 20-weeks gestation. Twin pregnancy was subsequently proven radiologically.

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She was examined vaginally at weekly intervals from the 10th week onwards but the cervical canal only admitted the tip of the finger on each occasion.

On the 15th December, 1958, at approximately 19-weeks gestation (uterine size equivalent to a 26-weeks gestation), she was recommended for admission to hospital for prophylactic cervical ligation. By the time of operation, 6 days later, it was found that the internal os had dilated sufficiently to easily admit the forefinger. The forewaters were not as yet bulging.

The cervix was ligated with one strand of No. 6 black silk in a similar manner to the modified Shirodkar technique as described by Green-Armytage and McClure Browne (1957). The cervix was grasped by two anterior and two posterior sponge holding forceps and a transverse incision was made across the front of the cervix at the cervico-vaginal junction. The bladder and its fascia were then reflected upwards to expose the region of the internal os. A similar incision was made posteriorly and the fascia and peritoneal cul-de-sac were reflected upwards also. The suture, on a large round bodied needle, was then inserted. It was commenced through the posterior vaginal incision and passed anteriorly around the cervical fibro-muscular tissue on the left side. It was beneath the vaginal mucosa on that side and pierced the insertion of the cardinal ligament. It emerged from the anterior vaginal incision and was passed across the front of the cervix. It was then passed posteriorly around the cervix on the right side at the same depth and brought out through the posterior vaginal incision where it was tied securely. At the end of the procedure the internal os was closed. The vaginal incisions were loosely approximated with interrupted No. 00 catgut sutures. The slight oozing was controlled by a roll of gauze packed into the vagina for 24 hours. A catheter was left indwelling during this time. After a 10-day rest period in hospital with antibiotic cover she was discharged and again examined vaginally at weekly intervals in the Antenatal Clinic.

On the 9th February, 1959, at approximately 26-weeks gestation (uterine size equivalent to 34-weeks gestation), it was noted that the cervical suture which had been more readily palpable at each examination had now cut through to the cervical canal on the right side. The internal os was dilated to one finger's breadth. She was again admitted to hospital and a second suture of No. 6 black silk was inserted, again by the modified Shirodkar technique. The first suture was left *in situ*.

She remained at bed rest in hospital until 2nd March, 1959, weekly vaginal examinations being performed. At this time at approximately 30-weeks gestation (uterine size equivalent to 36-weeks gestation), it was noticed that she was draining small amounts of clear liquor. A vaginal examination revealed that the second suture had now cut through the cervix on the right side and was also palpable in the cervical canal. A foetal head and the membranes were pressed against this suture and the internal os had dilated to one finger's breadth. Occasional uterine contractions had also been noticed by the patient.

She was again taken to the operating theatre. The first suture which was no longer giving support to the internal os was removed. The second suture which had eroded the right cervical wall and entered the canal on that side was still considered to be affording some support and was therefore not removed. A third suture was now inserted, using the purse-string type suture described by McDonald (1957). This suture was placed somewhat higher than would be possible in the operation described by McDonald unless, as in this case, the bladder had been recently reflected. At the end of the operation, the internal os was closed to about 3 mm. diameter.

On her return to the ward she was heavily sedated for 48 hours. Antibiotics were commenced (Chloramphenicol, 2 g. per day and Erythromycin, 2 g. per day). These doses were halved after 4 days. The only sign that transient intra-uterine infection may have occurred during the first post-operative week was a tachycardia which gradually settled over 6 days. There was no pyrexia.

Contractions continued intermittently during the next 24 hours. On the 3rd March, 1959, she was given intravenous progesterone (Proluton, intravenous—Schering), 20 mg. and this was repeated after 6 hours. She was also given 17-α-hydroxyprogesterone-caproate (Proluton Depot —Schering), 250 mg. by intramuscular injection.

There was no apparent change in the strength or periodicity of the uterine contractions.

On the 4th March, 1959, after uterine contractions had been present for 48 hours she was given relaxin (Releasin—Warner-Chilcott) 40 mg. intramuscularly and then 20 mg. intramuscularly 4-hourly for three doses. Shortly after the first injection, it was noticed that the uterine contractions were weaker and more intermittent than previously and after a further 4 hours they had almost disappeared.

She remained at bed rest, with only occasional contractions and slight drainage of liquor amnii until the 11th March, 1959, at 31-weeks gestation (uterine size equivalent to 38-weeks gestation) when the uterine contractions recurred. A similar regime of relaxin was again commenced but this time it was without effect on the contractions, which were occurring regularly every 3 minutes and lasting approximately 40 seconds.

She was transferred to the labour ward where a vaginal examination revealed the internal os to be one finger's breadth dilated; the second suture was in the cervical canal on the right side and the third suture could be palpated by a finger in the canal, still within the cervix but separated from the finger by only a thin layer of cervical tissue. Both sutures were cut and removed. After their removal the internal os dilated sufficiently to admit 3 fingers.

Labour proceeded satisfactorily and after a further 5 hours, 2 female living premature infants were delivered. Episiotomy had been performed. The third stage of labour and the puerperium were normal.

The birth weights of the infants were 3 pounds 1 ounce and 2 pounds 15¾ ounces and both subsequently survived.

Discussion

The patient's first 2 pregnancies had ended in premature labour following spontaneous rupture of the membranes at 28-weeks gestation. During her third pregnancy, an incompetent internal os was confirmed by the presence of cervical dilatation and bulging of the forewaters at 27-weeks gestation and this had been treated successfully by cervical ligation.

The cervix was ligated prophylactically in the pregnancy under discussion at 19-weeks gestation because of the uterine size which was equivalent to a 26-weeks gestation. It was again ligated at 26-weeks gestation because the suture had cut through the cervix and had entered the canal on the right side. It was considered that this suture was no longer adequately supporting the internal os. The second suture after a further 4 weeks also cut through the cervix and entered the cervical canal. I believe it was this suture which was responsible for perforation of the membranes, as at vaginal examination the foetal head and membranes were pressing against the part of the suture that was drawn across a segment of the canal. I believe that, had each suture been removed as soon as it was palpable in the cervical canal and another suture inserted, the membranes would not have been ruptured and pregnancy could have been further prolonged.

A third suture was inserted at this time, in spite of the fact that the membranes were ruptured. The internal os was not completely closed at operation, so that liquor was still able to drain freely. As a general rule I do not believe it good practice to suture the cervix once the membranes have ruptured as the results are usually poor and the danger of intra-uterine infection must be increased. In this case, however, with premature twins at 30-weeks gestation, it was felt that, if the cervix could be prevented from dilating, the onset of labour might be delayed for even a short time and the advantage in terms of increased foetal maturity thus justify the operation.

The uterine contractions that were present at the time of the third ligation and during the succeeding 48 hours were difficult to control. Heavy sedation had no effect. Intravenous progesterone combined with 17-α-hydroxyprogesterone caproate was used in an attempt to bring about uterine quiescence but this was also of no avail.

Since Abramson and Reid (1955) demonstrated that administration of relaxin to patients with threatened premature labour was followed by cessation of uterine contractions, this extract has been used in a number of cases in this hospital. The overall results have been disappointing but in this case it appeared to cause marked

diminution in the frequency and strength of contractions. These had been present for 48 hours prior to its administration and almost disappeared within 2 hours of the first injection. The association seemed to have been too close for coincidence. It should be stated, however, that on the latter occasion, when labour commenced, relaxin was quite ineffective in stopping the contractions.

It can be seen from this case that an important complication of cervical ligation is the tendency for the suture to cut through the cervical tissue until one part of it is stretched across the cervical canal; at which time its efficiency as a support for the internal os ceases. It is also suggested that this suture in the cervical canal is a potential danger to the intact membranes.

It would appear, therefore, that the essentials of successful ligation are, firstly, to place the suture around the cervix as far away from the canal as possible, secondly, to use suture material that is least likely to cut through the cervix and, finally, by frequent observation, to detect as soon as possible a suture that has entered the cervical canal and replace it with another correctly positioned suture.

At first glance, it would appear that the "purse-string" type suture as described by McDonald has much to recommend it, in that the suture has to traverse vaginal mucosa as well as cervical fibro-muscular tissue in its passage towards the cervical canal; but more important still is the fact that the operation is simple to perform and does not entail opening of tissue planes and reflection of the bladder. These advantages are somewhat nullified by the tendency of the suture to pull out, and this occurred in 6 of McDonald's series of 70 cases. However, the main objection to the McDonald "purse-string" suture operation is that, because the bladder is not reflected upwards, the suture cannot be placed at a high enough level on the cervix. The modified Shirodkar technique has the advantage of bladder reflection and the suture can therefore be placed nearer the level of the internal os. Even after bladder reflection it is often difficult to reach this level. The "purse-string" suture was used in this case only on the third occasion as the bladder had remained at a high level following the previous two operations and it was considered that it could be placed at a high enough level without further reflection.

The tendency for the suture to cut through the cervix is due to the taking up of the isthmus and formation of the lower uterine segment which inevitably occurs as pregnancy proceeds (Shaw and Nirula, 1951). Should abnormal contractions be present also, as occurs in threatened premature labour, then this tendency is accentuated. It has been the practice in this hospital to use non-absorbable suture material and to remove the suture at the 38th-week of pregnancy or when labour commences, should this occur earlier. We believe this to be a preferable procedure to Caesarean section without removal of the suture, provided the results in terms of infants saved are as good as those following the more permanent forms of cervical repair and ligation, and at the moment we believe this to be the case. The search for the best suture material therefore continues. It seems reasonable to assume that the thicker the material used, the less is the chance of it cutting through. Number 6 black silk was used on 2 occasions, in this case, and No. 12 haemorrhoidal silk on the other occasion. (These were the thickest suture materials available at the time of each operation.) McDonald recommends No. 4 Mersilk which is the thickest form of this brand of braided silk available. Shirodkar (1955) and Barter *et al.* (1958) have used strips of fascia lata and claim good results. Caesarean section, however, is usually necessary after this form of ligation. More recently Barter has used a non-absorbable Dacron material called Mersaline. This is in the form of a tape $\frac{1}{8}$ of an inch wide and he claims it to be more satisfactory than the fascial strips. Shirodkar has also recently used a similar nylon tape with apparently good results. The advantage of these tapes is that their flatness and width diminishes the cutting tendency and provided they can be satisfactorily removed prior to labour (and on this point we have as yet had no experience) they would appear to constitute the ideal suture material.

Finally, the danger to the intact membranes of a suture drawn across a segment of the cervical canal has been stressed. It is considered that such a suture was the cause of rupture of the membranes in the case presented.

Summary

(1) Living twin premature infants were delivered at 31-weeks gestation (after 3 cervical ligations) in a case of proven incompetent internal os.

(2) Labour was delayed for a week by the insertion of the third cervical suture following rupture of the membranes. Uterine contractions appeared to be successfully controlled by the administration of relaxin.

(3) The various techniques for cervical ligation are briefly discussed. The modified Shirodkar technique as described by Green-Armytage and McClure Browne is considered preferable to the "purse-string" suture described by McDonald.

(4) The danger to the intact membranes of a suture which has cut through the cervix and is lying across the cervical canal is stressed.

Addendum

Since submission of this paper for publication, Mersaline tapes have been used in a number of cases in this hospital. They have been found to be comparatively easy to insert and remove and, in the opinion of those surgeons who have used them, appear to have a minimal cutting tendency. It is the writer's opinion that these tapes are at the moment the ideal suture material.

Acknowledgments

I should like to thank Professor Bruce Mayes, under whose care the patient was admitted to hospital, for permission to report the case and Drs. James Farrar and Alan Bradfield for helpful criticisms in the preparation of the paper. I should also like to thank Miss Maureen Marshall, of the Medical Record Department, for her help.

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INCIDENCE OF THE SUPINE HYPOTENSIVE SYNDROME IN LATE PREGNANCY

A Clinical Study in 500 Subjects

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A TENDENCY of women in late pregnancy to experience a fall in blood pressure when supine has probably been noted by many observers but only few references to this syndrome have appeared in the literature. In a recent report, Winzeler (1958) reviews fully the existent information on the subject. The hypotension which may develop is probably the result of compression of the inferior vena cava by the gravid uterus with consequent impairment of venous return to the heart (Brigden, Howarth and Sharpey-Schafer, 1950). Furthermore, there is evidence that marked lumbar lordosis, commonly seen in late pregnancy, may predispose to occlusion of this vein (Bull, 1948; Brigden *et al.*, 1950).

This type of postural hypotension is of some moment because the signs can simulate true ante-partum shock and, in the presence of accidental haemorrhage, confuse the clinical picture. It has been suggested that the rise of venous pressure resulting from compression of the inferior vena cava may cause premature separation of the placenta (Howard and Goodson, 1953; Mengert, Goodson, Campbell and Haynes, 1953). Of particular interest to anaesthetists is the fact that a change from the lateral to the supine posture may be the main cause of sudden circulatory collapse and death when spinal analgesia is employed for Caesarean section (Holmes, 1957; Williams, 1958; Holmes, 1960).

McIntosh Marshall (1939) concluded from an extensive review that with the use of spinal analgesia for Caesarean section a maternal death rate of at least one per cent was inevitable. In view of this, it was thought of interest to ascertain whether the occurrence of profound hypotension in pregnant women, when supine, was of such frequency as might account for a one per cent mortality in such patients when subjected to the additional influence of spinal blockade with its associated sympathetic paralysis.

A study of the literature yields little information as to the incidence and variation in intensity of this peculiar predisposition to postural hypotension. de Rezende (1950) observed 50 women in late pregnancy for 15 minutes in the lateral and a similar period in the supine position. While these subjects were supine, a marked fall of blood pressure and tachycardia was noted in 7 and lesser degrees of hypotension in a further 8; 5 of the 7 in the former group developed syncope with bradycardia. Of the 35 women who exhibited no significant change in blood pressure, 2 showed bradycardia and 5 "subjective signs of intolerance". McRoberts (1951) also compared blood pressures in the supine and lateral postures in 50 pregnant women. He considered that the series was too small to draw definite conclusions but he observed that the blood pressure frequently fell in the supine position. The stage of gestation at which these studies were carried out is not recorded. Howard, Goodson and Mengert (1953) noted the syndrome in 18 out of 160 women at term (11·2 per cent) but the incidence of different degrees of hypotension observed by them is not stated.

Method of Investigation

Five hundred women, all pregnant for 36 or more weeks, were examined in the course of their routine antenatal visits. Of these, 180 were parous and 320 primigravidae. One hundred and six subjects were examined more than once, the total number of antenatal studies being 616. In addition, those women who had exhibited marked falls of blood pressure were examined again some days after delivery. Circulatory and subjective changes were recorded.

The subjects lay in the supine posture on an examination couch and blood pressure and pulse estimations were obtained at minute intervals for six minutes or occasionally longer when marked falls of pressure were observed. Following this, pulse and blood pressure readings were continued in the lateral position.

Results

The frequency and extent of falls in systolic blood pressure observed in the supine posture are presented in Table I. It was thought convenient to divide the degrees of hypotension into six grades. Among the 148 subjects who experienced no fall in systolic pressure or only an insignificant one (grade I), 45 exhibited, however, a rise in diastolic pressure of 50 per cent or more. In 3 subjects showing this type of response there was marked bradycardia and a reduction in pulse pressure to between 5 to 10 mm. Hg (Fig. 1). When the systolic pressure fell by more than 50 per cent (grade VI) the pulse rate, after an initial rise, dropped precipitously (Fig. 2), while a grade IV or V fall was accompanied by

Table I

Incidence and Degree of Hypotension Induced by Supine Posture

Fall in Systolic Pressure (per cent)	No. of Patients	Percentage of Total
<10·0 (Grade I)	148	29·6
10–19·9 (Grade II) ..	194	38·8
20–29·9 (Grade III) ..	117	23·4
30–39·9 (Grade IV) ..	23	4·6
40–49·9 (Grade V) ..	8	1·6
>50·0 (Grade VI) ..	10	2·0
Total	500	100·0

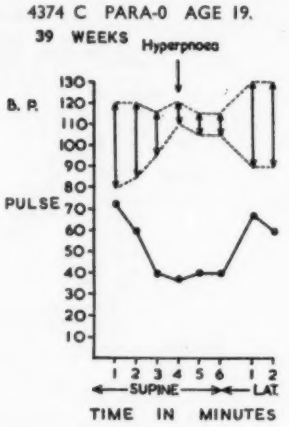

Fig. 1

Shows marked reduction in pulse pressure without significant change in systolic pressure. The degree of bradycardia suggests deficiency in venous return but systolic pressure was maintained by compensatory vasoconstriction.

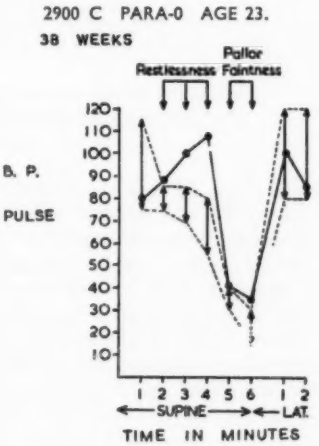

Fig. 2

Shows supine hypotension grade VI with bradycardia. This circulatory response signifies grave deficiency in venous return.

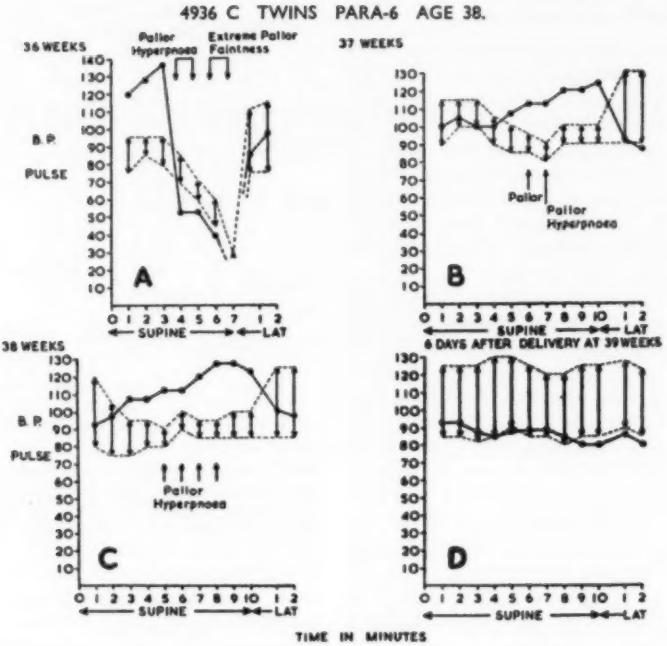

FIG. 3

Shows that lowering of the uterine fundus at 37-weeks gestation (B) resulted in mitigation of the syndrome. There was no supine hypotension after delivery (D).

tachycardia (Figs. 3B and C). Hypotension of grades III to VI was always attended by a marked reduction in pulse pressure.

Serious hypotension usually occurred before 39 weeks gestation. Falls of systolic pressure of grade V and VI (18 subjects) were observed only once at 39 and 3 times at 40-weeks gestation and in all 4 cases the foetal head was still free above the pelvic brim. The type of response shown in Fig. 1 occurred once at 37 and twice at 39-weeks gestation; in all 3 cases the foetal head was high. Repeated examinations during the last month of pregnancy showed that supine hypotension tended to become less marked as term approached. Figures 3A, B and C illustrate this point in a woman who volunteered the information at 37 weeks (3B) that "her womb had dropped" since her previous visit (3A). In another subject (Figs. 4A, B and C) the foetal head was still free at 39-weeks gestation and it will be noted that supine hypotension was still marked at that time (Fig. 4C). In all cases the syndrome had completely disappeared after delivery (Figs. 3D and 4D).

A number of signs and symptoms of intolerance to the supine position were noted in connexion with various degrees of hypotension, namely restlessness, hyperpnoea, pallor, desire to flex hips and knees, dizziness and faintness. Some subjects refused to remain supine for the full period of the experiment, others appeared to faint and had to be helped into the lateral position.

DISCUSSION

The likelihood of circulatory collapse occurring in a patient undergoing Caesarean section

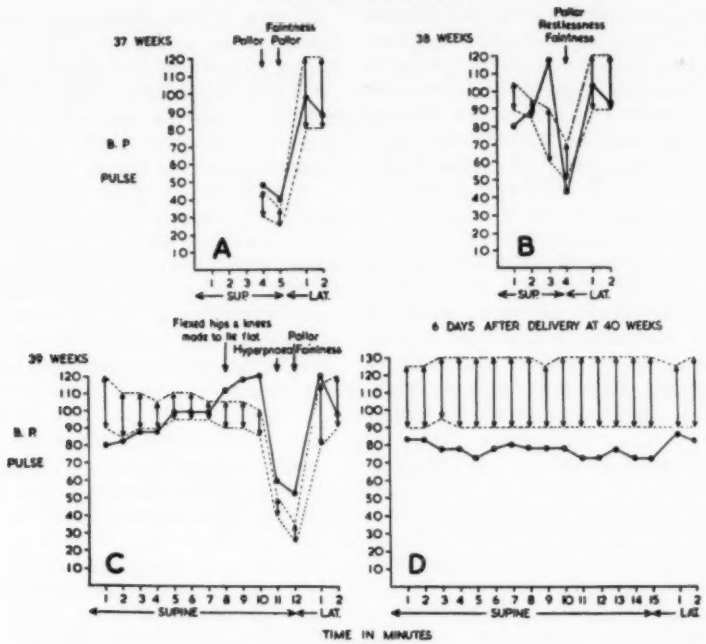

FIG. 4

Shows that, when the foetal head was free at 39-weeks gestation (C), the syndrome was still present. There was no supine hypotension after delivery (D).

under spinal analgesia exists whenever marked supine hypotension is elicited before operation. If sympathetic paralysis is kept minimal by restricting the dose of analgesic agent and avoiding barbotage, a dangerous fall of blood pressure need only be anticipated in patients who previously exhibited a hypotensive response of grade V or VI. Eighteen (3·6 per cent) of the subjects under investigation came into this category but it must be remembered that in the majority the syndrome became less severe after 38-weeks gestation. How many subjects would have developed dangerous hypotension, had they undergone spinal block for abdominal section depended on the stage of pregnancy at the time of operation. In the group under review only 4 subjects exhibited grave postural hypotension at or near term.

Figure 1 illustrates an interesting aspect of the problem. Although the development of bradycardia so profound as that occurring with hypotension of grade VI (Fig. 2) signifies a serious deficiency in venous return, systolic pressure was probably maintained by compensatory vasoconstriction. It seems likely therefore that this type of response will lead to grave hypotension as a result of spinal analgesia, because the inevitable sympathetic blockade will prevent vasoconstriction.

A likely explanation why the hypotensive syndrome tended to become less marked as term approached was found when it became apparent that this change could be related to the descent of the foetal head into the pelvis. It will be recalled that such a relationship was noted in the subjects who were examined repeatedly during

the last month of pregnancy (Figs. 3 and 4). Compression of the inferior vena cava appears to occur only at a level just below the diaphragm and once the foetal head becomes engaged in the pelvic brim the fundus of the uterus will come to lie below that point. This may explain why the syndrome is often relieved suddenly and why it has rarely been noted once labour has begun. The reason for individual differences in intensity of supine hypotension will be found mainly in variable anatomical features, such as the distance between 12th dorsal and 1st sacral vertebrae, the degree of lumbar lordosis and the size or degree of tonicity of the uterus. However, individual differences in vasomotor control may also be important as shown by subjects who exhibit a markedly reduced pulse pressure and bradycardia without significant change in systolic pressure.

One or more of the subjective signs and symptoms of intolerance to supine posture were invariably noted with grade V and VI hypotensive responses and with the type illustrated in Figure 1. However, restlessness and flexing of hips were not uncommonly observed with lesser grades of hypotension. A few excitable subjects refused to remain supine for the full period of the study. Hyperpnoea and flexing of the hip joints may be manifestations of reflex action to improve the inadequate venous return, the former through augmenting the effect of the "respiratory pump" and the latter by lessening lumbar lordosis. All these reactions at times raised the blood pressure or arrested its decline. Some subjects complained of dizziness even though the fall of pressure was comparatively slight. Intense pallor always accompanied profound hypotension. The level of systolic pressure at which subjects appeared to faint was about 40 mm. Hg.

Summary

(1) The supine hypotensive syndrome was studied in an unselected group of 500 women during the last month of pregnancy.

(2) The hypotension observed in these subjects was classified as six grades and the incidence of grave hypotension (grade VI) was found to be 2 per cent.

(3) In 45 subjects (9 per cent) a marked rise in diastolic pressure without significant change in systolic pressure was noted. In 3 of these there was a reduction in pulse pressure to between 5 to 10 mm. Hg and profound bradycardia.

(4) Postural hypotension often became less marked as term approached and this change could be related to the descent of the foetal head into the pelvis.

Acknowledgment

I wish to thank Professor Robert Kellar and his staff for their courtesy and co-operation during this investigation.

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THE AETIOLOGY AND SIGNIFICANCE OF CONGENITAL HEART BLOCK

(The Report of a Case Studied by Serial Section of the Heart)

BY

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CONGENITAL heart block is an uncommon condition. Moxon's case (1879) reported by Campbell and Suzman (1934) was almost certainly an example of congenital heart block associated with pulmonary stenosis and an interventricular septal defect. But the clinical entity was first recognized by Morquio in 1901 and the first authenticated case was reported by Van der Heuvel in 1908. Since then just over 100 cases have been recorded in the literature (Turner, 1947). McNie and Johnstone (1959), reviewing the literature, found 14 cases in which the diagnosis of complete heart block had been made before the baby was born. In a few other cases an antenatal diagnosis of incomplete heart block has been made (Geiger and Hines, 1940; Dunn, 1952). As several other authors have suggested, these figures probably do not represent the true incidence of the condition or its detection antenatally. Many other cases have probably not been recorded.

The study of the conducting mechanism of the heart began with Purkinje in 1845, and in 1893 His described the atrio-ventricular bundle. It was Tawara in 1906 who first described the atrio-ventricular node and also the connexion between the bundle of His and the ventricular muscle fibres. Mall (1911), and more recently Walls (1947), have studied the development of the conducting tissues of the heart. Keith (1909) described the anatomy of the bundle of His in relation to various congenital abnormalities of the heart and great vessels. Histological studies of the course of the atrio-ventricular bundle in relation to congenital defects of the heart have been made by Reemtsma and Cobenhaver (1958). Up to the present, histological examination of the conducting mechanism in cases of congenital heart block has been made in only 7 cases. Donoso *et al.* (1956) mention 7 cases which were studied by serial section of the heart, but they omitted to include one of the 2 cases described by Wallgren and Winblad (1937). They quote, however, a case described by Wendkos and Study (1947), in which it is stated that the section of muscle failed to show anything which could be identified as a bundle of His. No mention is made that serial sections were cut. Lev *et al.* (1958) state that 9 such studies have been made in cases of congenital heart block, but only 7 could be found on consulting their references. This report describes the eighth case to be studied by serial section. It is considered to be of interest because the antenatal diagnosis of the condition and its differentiation from other causes of foetal bradycardia, and in particular foetal distress, is important (Redman, 1958). Secondly, this paper has been written because the pathological anatomy of congenital heart block still stands in need of fuller description. Recent attempts to repair septal defects have been complicated by the appearance of post-operative heart block (Cooley *et al.*, 1957; Clark *et al.*, 1959), and in this respect more precise knowledge of the anatomy of the conducting system in relation to septal defects is needed.

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Case Report

Mrs. J. T., aged 37, had had 3 previous normal pregnancies ending at full term in spontaneous delivery of living children, all of whom are healthy. She was first seen at Perivale Maternity Hospital on 9th May, 1957, eight weeks after her last normal menstrual period. On general examination no abnormal physical signs were found. Her blood pressure was 140/80. The presence of a normal pregnancy, consistent with the duration of amenorrhoea, was confirmed on pelvic examination. The Wassermann reaction was negative. The patient had no febrile illness immediately before or during pregnancy and, as far as was known, she never came into contact with any infectious disease. She attended the antenatal clinic regularly. On abdominal examination it was repeatedly noted that the uterus failed to increase in size at the expected rate. At 36 weeks the fundus of the uterus reached half-way between the umbilicus and the xiphisternum. The vertex was presenting and not engaged. On auscultation it was noted that the loud and regular foetal heart was very slow. It beat at 68 per minute and the maternal pulse recorded at the same moment by another observer was 92. A week later the foetal bradycardia was still present. She had developed oedema of the ankles and her blood pressure was 150/90. She was admitted to hospital for antenatal rest and observation. The foetus continued to present as a vertex, but it remained small and grew slowly. The foetal heart was never observed to beat faster than 78 per minute and it was always regular. A presumptive diagnosis of congenital heart block, probably in association with other major defects, was made. An X-ray of the abdomen taken during the 39th week showed a small but otherwise apparently normal foetus. At 42 weeks the patient was not in labour. The blood pressure had remained at 150/90, although the oedema had subsided and there was never any albuminuria. Surgical induction of labour was performed by puncturing the hindwaters and 4 ounces of clear liquor were withdrawn. Five days later labour commenced. The first stage lasted 4 hours and the second stage of labour took 10 minutes and ended in a spontaneous vertex delivery. Throughout labour the foetal heart remained strong and regular in rate and rhythm, but it never rose above 72 beats per minute. The third stage was uneventful and the placenta and membranes were normal.

The baby, a living female, weighed 5 pounds 2 ounces (2,325 g.) and was in a state of marked blue asphyxia. Regular respiration was established 2 minutes after birth. Following mucus extraction and the administration of intra-nasal oxygen, her colour gradually improved and she cried.

The baby was 19 inches long (47·5 cm.). The head was scaphocephalic and the occipito-frontal circumference measured 12¼ inches (31·75 cm.). The sutures and fontanelles were almost closed. The palpebral fissures were narrow with marked epicanthic folds. The ears were set low on the side of the head and the neck was webbed. The upper limbs were atonic. Both hips were dislocated and there was a severe degree of bilateral calcaneo-valgus. The heart beat regularly at 60 per minute. No murmurs were heard. The lungs were well aerated. The abdomen was normal. Urine and meconium were passed shortly after birth.

For the remainder of the baby's life slight cyanosis persisted and it increased markedly when she cried. She was lethargic and made little spontaneous movement. Three days after birth the cyanosis increased and the respiratory rate rose. The heart rate remained at 60 per minute. The baby's condition rapidly deteriorated and she died 70 hours after birth.

Post-Mortem Findings

Apart from the deformed lower limbs and the curious head (already described), no other abnormality was found on external examination or on internal examination of the abdomen or cranium. The lungs were poorly aerated. A few petechial haemorrhages were found on the pleurae and pericardium.

Externally the heart was of normal shape and size. It weighed 16 g.; Potter (1952) gives an average weight of 14·5 g. for the heart of a child weighing 2,250 g. The heart measured 5×5·6×2·8 cm. The pericardium was normal. The right atrium and ventricle were dilated. The left ventricle was small. The wall of the right ventricle was 3 mm. thick and that of the left ventricle 2 mm. The myocardium and endocardium appeared healthy. There was a defect in the membranous part of the interventricular septum measuring 1·5×0·8 cm. (Fig. 1). The foramen ovale was closed. The ductus arteriosus was patent, but normal for a child of this age. Potter (1952) states that the ductus is about 8 mm. in diameter in the first 2 days of life (Wilson, 1958). The mitral, tricuspid, aortic and pulmonary valves were normal. The aorta was overriding the right ventricle very slightly. The great vessels arose normally from the arch of the aorta.

Serial Section of the Heart

A block was prepared from the heart, including the whole of the muscular and membranous portions of the interventricular septum and the atrial septum up to the level of the annulus ovalis (to include the fossa ovalis and the openings of the inferior vena cava and the coronary sinus: Figs. 2 and 3). The tissue was fixed in formalin and, after clearing, embedded in paraffin wax. Serial sections, 10 microns thick, were cut from the block through the vertical axis of the heart and at right-angles to the interventricular septum, beginning at the right border of the heart. The sections were mounted in sequence. Every 4th section was stained with haematoxylin and eosin, and every 5th section was stained with Van Gieson's.

The atrio-ventricular node was not identified (possibly owing to poor fixation of the atrial musculature). The conducting tissue was first identified in section 900. (The location of sections can be determined by reference to the vertical lines superimposed on the photographs of the block in Figures 2 and 3.) Section 900 showed a bundle running vertically in the central fibrous body, which separates the atrial and ventricular musculature. As the bundle was followed through the central fibrous body it became split into disconnected strands of loose rather myxomatous fibrous tissue (Fig. 4). Section 1104 showed the bundle well defined, but the direction of the fibres had changed so that they now ran horizontally, although longitudinal strands could still be seen entering the superior aspect of the bundle from the central fibrous body (Fig. 5). The bundle was easily distinguished from the adjacent cardiac muscle. The former consisted of loosely packed and more slender fibres with small nuclei and paler staining cytoplasm (cf. Keith and Flack, 1906). A loose sheath of fibrous tissue was condensed around it and in every section one or two blood vessels could be seen within the bundle (Fig. 6). The bundle continued to run horizontally in the central fibrous body just proximal to the ventricular muscle mass. Section 1280 (Fig. 7) showed a rearrangement of the fibres within the bundle. This marked the origin of the bundle branches. Examination of sections higher in the series enabled the left bundle branch to be followed downwards until it finally terminated as a sheet of Purkinje fibres beneath the endocardium of the left ventricle. After the left bundle had split off the right bundle branch entered the main muscular mass of the ventricular septum and followed a downwards course towards the right side of the septum. At section 1425 the defect in the membranous part of the interventricular septum began. Further study of this section showed that the atrio-ventricular bundle had already divided. At this level the left bundle branch had disappeared and was represented only by Purkinje fibres. The right bundle branch was clearly visible intact and within the ventricular muscle mass beneath the endocardium of the right ventricle (Fig. 8). Subsequent sections showed that the intact conducting system always lay a considerable distance below the interventricular septal defect. The right bundle branch terminated as a network of subendocardial Purkinje fibres (Fig. 9).

Discussion

The Diagnosis of Congenital Heart Block. Unfortunately electrocardiographic recordings of this baby's heart were not made either before or after delivery. But, according to Potter (1952), a foetal heart rate of less than 80, before the onset of labour, is strong evidence in favour of the diagnosis of heart block. Taussig (1947) considers that the idioventricular rate of the newborn is 80. Yater (1929) accepted the congenital origin of heart block if it had been established by graphic means in the very young and if a slow pulse rate had been noted at a relatively early age and a history of infection was absent. But Yater accepted Perotti's case (1928) without graphic recordings because bradycardia had been present since birth. Campbell and Suzman (1934) and Wallgren and Winblad (1937) also accept the congenital origin of heart block in the absence of graphic recordings in patients in whom the bradycardia has been noted soon after, at or before birth. The case described here can therefore be accepted as one of congenital heart block, since for a period of 6 weeks before birth and for 3 days of life the heart rate was never observed to be faster than 78 per minute. The degree of heart block, however, remains in

doubt. The antenatal diagnosis of heart block is obviously of importance. During labour the foetal bradycardia might be interpreted as foetal distress, leading perhaps to unnecessary surgical intervention (Devitt and Pinto, 1957; Redman, 1958). It is suggested that, when an abnormally slow foetal heart rate is noted before the onset of labour, the diagnosis of congenital heart block should be considered and if possible confirmed or excluded by foetal electrocardiography (Smyth and Farrow, 1958; Larks, 1959). However, a rate of 80 or less before the onset of labour, can be considered pathognomonic of heart block.

Aetiology. The causes of congenital heart block fall into two groups, prenatal infections causing myocarditis and anatomical abnormalities of the heart.

Prenatal infection as a cause of congenital heart block is not an important factor. In the literature 2 cases have been described in association with fibroelastosis (Stadler *et al.*, 1950; Devitt and Pinto, 1957). In another case of congenital heart block, toxoplasmosis had produced a myocarditis (Kleine and Wolffram, 1957). Congenital syphilis has been suggested as a possible cause, but a search of the literature has not revealed a reported case. None of these conditions was present in the case under discussion. The Wassermann reaction was negative and complement-fixation and dye tests for toxoplasmosis on the maternal serum were also negative.

In the vast majority of cases congenital heart block is caused by a defect in the development of the heart. Some authorities state that most cases are due to a septal defect (Wendkos and Study, 1947; White, 1951). It is submitted that septal defects *per se* are not the cause of congenital heart block. Wallgren and Winblad in 1937 found that 51 of the 77 cases reported at that time, were reputed to have an interventricular septal defect. However, Donoso *et al.* (1956), in a review of the literature, found that only 12 of the 17 cases of congenital heart block examined post-mortem, had an interventricular septal defect. The clinical diagnosis of septal defects is notoriously difficult even after exhaustive investigations have been performed. Conversely, interventricular septal defects are amongst the commonest of cardiac malformations, but in the series that have been reported congenital heart block has been an unusual finding. Thus, Brown (1951) found no case of heart block in 200 patients with an interventricular septal defect. Other malformations of the heart and great vessels have been reported in association with congenital heart block almost as frequently as septal defects.

Anatomical evidence also supports the view that the two lesions are independent of each other. The conducting system of the heart has been demonstrated in the 8 mm. embryo during the 5th week of foetal life, when the heart is still bilocular, that is, 2 to 3 weeks before the atrial and ventricular septa have been completed (Mall, 1911; Walls, 1947). Further, Keith (1909), Monckeberg (1924) and Reemtsma and Cobenhaver (1958) have all shown that the bundle of His is present in hearts with septal defects, and that it runs posteriorly in the margin of the defect.

Pathological Anatomy. This is the eighth reported case of congenital heart block to be studied by serial section of the heart, in order to establish the site of the lesion. Table I summarizes the findings in these 8 reported cases. Heart block has been associated with a variety of cardiac anomalies and in one instance with an apparently normal heart. The lesion is almost identical in all these cases, namely interruption of the bundle of His below the atrio-ventricular node, as it passes through the trigonum fibrosum dextrum.

Developmentally the annuli fibrosi are formed from connective tissue which grows in to separate the atrial and ventricular musculature at the time when the endocardial cushions are fusing to effect division of the atrio-ventricular orifices. On the right side this fibrous tissue comes to surround the sole muscular link between atria and ventricles, that is the bundle of His, which pursues its course through that part of the fibrous skeleton of the heart known as the trigonum fibrosum dextrum. Now should the ingrowth of the connective tissue at this part of the atrio-ventricular junction depart in some way from normal it is not difficult to conceive that the bundle might be split up or even completely severed. If this supposition is true, such a lesion might exist independently or only coincidentally

FIG. 1

The heart opened—showing the interior of the left ventricle and the ventricular septal defect.

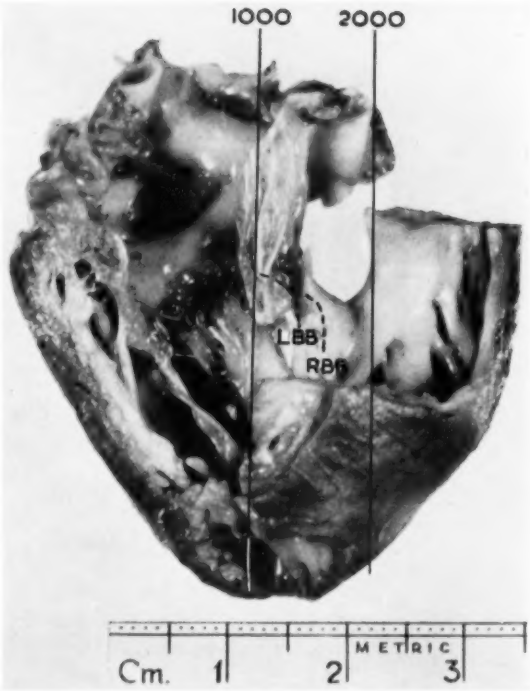

FIG. 2

Block prepared from the heart to show the right side of the ventricular septum. The vertical lines represent the locations of sections Nos. 1,000 and 2,000. (The course of the atrio-ventricular bundle has been superimposed on Figs. 2 and 3. It lies below the postero-inferior margin of the interventricular septal defect terminating in the left (L.B.B.) and right (R.B.B.) bundle branches.)

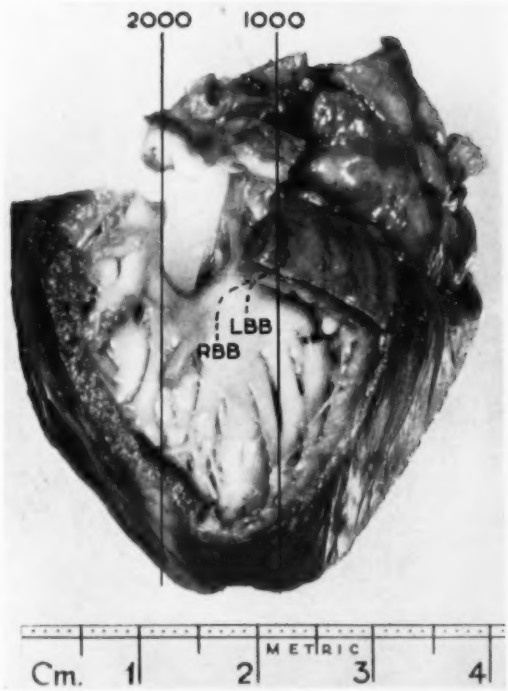

FIG. 3

Block prepared from the heart to show the left side of the ventricular septum. (Key as Fig. 2.)

P.J.H.

bundle branches.)

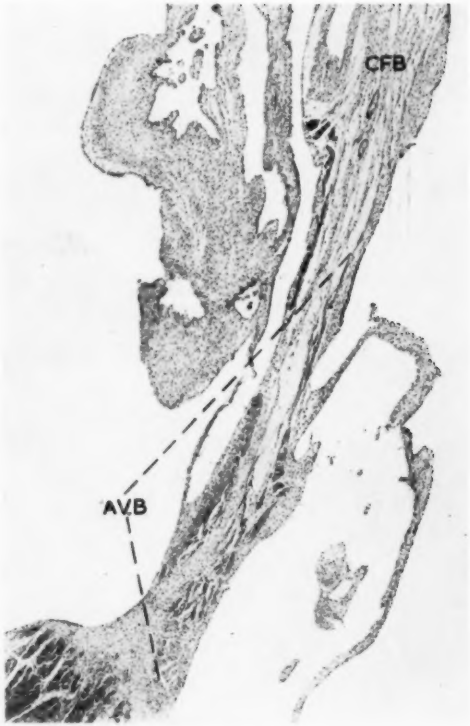

FIG. 4

Photomicrograph of section No. 1039 to show the atrio-ventricular bundle (A.V.B.) passing through the central fibrous body (C.F.B.). The bundle is split up into disconnected strands by myxomatous fibrous tissue. Magnification ×24. Haematoxylin and eosin.

FIG. 5

Photomicrograph of section No. 1104 to show the atrio-ventricular bundle (A.V.B.), now running horizontally as can be seen from the way in which the fibres have been cut transversely. Magnification ×24. Haematoxylin and eosin.

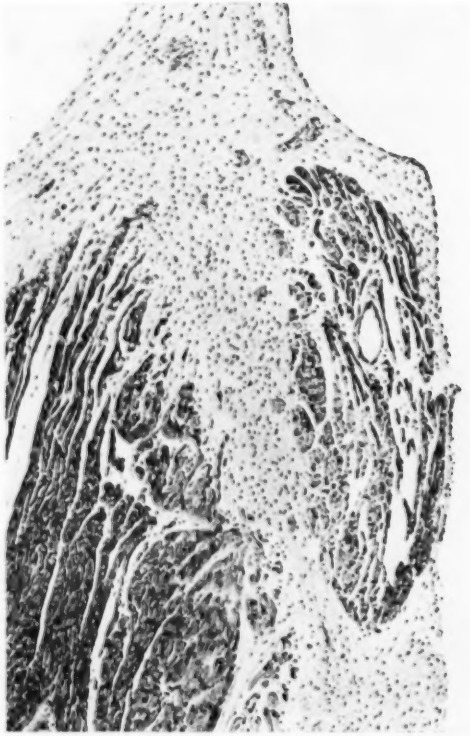

FIG. 6

Photomicrograph of section No. 1195. The bundle of His can be seen running transversely through the inferior part of the central fibrous body and just above the ventricular muscle mass. Magnification ×90. Haematoxylin and eosin.

FIG. 7

Photomicrograph of section No. 1280. This shows the fibres within the bundle of His arranged in 2 groups. It represents the origin of the bundle branches. A group of fibres is cut obliquely and runs downwards and to the left (L.B.B.), whilst the uppermost group of fibres are cut transversely and continue as the right bundle branch (R.B.B.). Magnification ×90. Haematoxylin and eosin.

right bundle branch (R.B.B.). Magnification ×90. Haematoxylin and eosin.

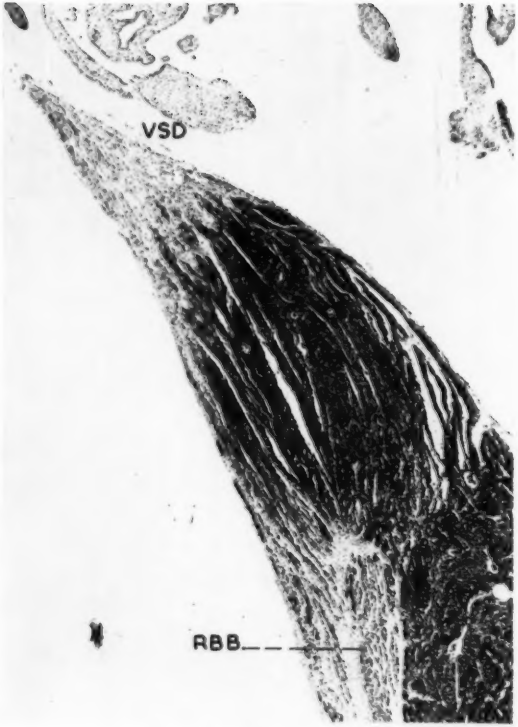

FIG. 8

Photomicrograph of section No. 1425 shows the beginning of the interventricular septal defect (V.S.D.) and a considerable distance below this the main muscle mass, the right bundle branch (R.B.B.), is clearly defined. Magnification ×22·5. Haematoxylin and eosin.

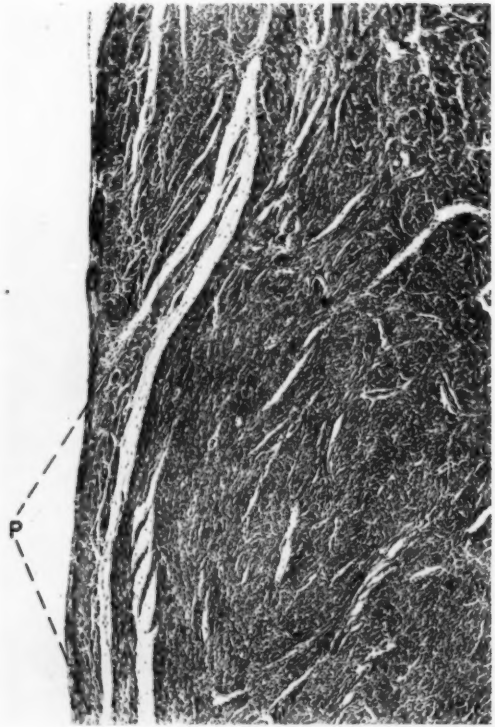

FIG. 9

Photomicrograph of section No. 1509 to show the Purkinje fibres (P) beneath the endocardium of the right side of the ventricular septum. Magnification approx. ×94. Haematoxylin and eosin.

TABLE I

Cases of Congenital Heart Block with Histological Studies of the Conducting System

Author	Sex	Age at Death	Heart	Conducting System
Wilson and Grant, 1925 ..	F	14 months	Large ventricular septal defect and pulmonary atresia	Bundle of His split into strands in the annulus fibrosus.
Yater, 1929	M	2 weeks	Transposition of atria and great vessels. Small ventricular septal defect	Bundle of His separated from atrio-ventricular nodes by a fibrous band immediately below it.
Yater *et al.*, 1933	M	2 months	Ventricular septal defect	Bundle of His separated from the node by fibrosis adjacent to septal defect.
Yater *et al.*, 1934	M	18 hours	Cor trioculare, biventriculare	Bundle of His divided from auricular muscle by fibrosis.
Wallgren and Winblad, 1937	F	2½ months	Normal heart	Bundle of His separated from the node by fibrosis.
Wallgren and Winblad, 1937	F	10 months	Persistent foramen primum	Degenerate and interrupted by fibrosis between node and bundle and bundle and branch.
Turpin *et al.*, 1947	M	6½ months	Rudimentary left ventricle	Rudimentary bundle of His entered septum; unidentified below it.
Author's case	F	70 hours	Ventricular septal defect	Bundle of His split into strands in the annulus fibrosus.

with other malformations of the heart. The findings in this case and the others reviewed in Table I lend support to this hypothesis. Certainly in cases of heart block the atrio-ventricular bundle is not interrupted simply by the presence of a defect in the atrial or ventricular septum. Superimposed on Figures 2 and 3 is the course of the atrio-ventricular bundle as it was found by study of serial sections cut from the heart described in this paper. The bundle runs undisturbed a considerable distance beneath the postero-inferior margin of the ventricular septal defect. The lesion which produced the heart block almost certainly lies in the central fibrous body, and was probably caused by excessive fibrosis in this area during early embryonic life.

SUMMARY

A case of congenital heart block, diagnosed ante-partum and associated with an interventricular septal defect, is described. The heart was studied by means of serial sections to determine the disposition of the conducting tissues.

The diagnosis, aetiology, and the pathological anatomy of congenital heart block are discussed and the literature is reviewed. The diagnosis of heart block should be considered if foetal bradycardia is noted before the onset of labour. Associated septal defects are not considered to be the cause of congenital heart block. It is suggested that the condition may result from defective formation of the central fibrous body of the heart whereby the developing conducting tissue is interrupted.

ACKNOWLEDGMENTS

I would like to thank Miss A. M. Dickins and Dr. J. Rubie for permission to publish the details

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THE ELDERLY PRIMIGRAVIDA

BY

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FROM a study of the literature it would appear that in recent years British authors have paid little attention to the subject of the elderly primigravida. Donald (1955) expresses surprise at this and appeals for a review of the problem. He quotes articles by Nixon and Miller, both published in 1931. More recent articles have been written by Dutta (1948) and Thompson (1951). On the other hand, American literature contains many references to the elderly primigravida (Randall and Taylor, 1949; Waters and Wager, 1950; Posner and Luftman, 1952).

The elderly primigravida has been variously defined. The majority of writers apply the term to a woman over the age of 35 years who is pregnant for the first time—she is in the last decade of her childbearing life. Miller and Nixon, however, both favour 40 years as the age at which a woman enters this group. Thompson divides his patients into those who are between 35 and 40 years and those who are over 40 years. In this report, a woman is so classed when aged 35 years or over.

A woman in this group, finding she is pregnant for the first time, requires more than the usual reassurance on many points, of which the following are of vital interest to her—"What are the chances of a normal pregnancy and confinement? Will the baby be normal?" The practitioner wants to know—"Are complications in the antenatal period more common in this group? Is labour likely to be prolonged? What is the incidence of instrumental delivery?" The following presentation is an attempt to answer these questions.

The case histories of 627 elderly primigravidae as defined, admitted to the Royal Maternity Hospital, Belfast, in the 10-year period 1947–1956 have been reviewed. In this period, 18,312 cases were admitted to the hospital, the incidence of elderly primigravidae being 3·3 per cent. All these cases were delivered or miscarried in the hospital. Cases admitted because of antenatal complications, e.g., severe pre-eclamptic toxaemia, but later delivered elsewhere, and those admitted with complications in the third stage or puerperium, following delivery outside the hospital, have been excluded.

TABLE I
Age at Delivery

Age (Years)	No.
35	146
36	95
37	96
38	72
39	57
40	46
41	35
42	18
43	12
44+	18

Of the 627 elderly primigravidae, 99 were emergency admissions including 32 abortions. Thus, 595 cases were delivered in hospital after the 28th week of pregnancy. There were 15 sets of twins and 1 set of triplets, giving a total of 612 infants.

Table I shows the age distribution of the patients. It should be noted that 129 patients (21·7 per cent) were over the age of 40 years. The oldest patient was 48 years of age. Table II shows the number of years that the patients had been married before delivery occurred. The

TABLE II
*Number of Years Married**

Years Married	No.
1	184
2	100
3	62
4	31
5	34
6	20
7	25
8	15
9	14
10	18
11	12
12	13
13	2
14	7
15	9
16	3
17	1
18	1
19	1

* This was not recorded in 43 cases.

longest period was 19 years (this patient had an uneventful pregnancy and a normal delivery at term).

Table III shows the previous gynaecological and medical history of the patients. Twenty-six had been investigated for infertility. Eleven had had myomectomy performed. In only 1 case did the previous myomectomy influence the method of delivery—where a prophylactic forceps delivery was carried out after 1 hour in the second stage. Of the other 10 cases, 6 forceps deliveries and 1 Caesarean section were carried out because of other indications, 1 had a normal delivery and 2 aborted.

In addition to the 11 patients, who had a myomectomy performed, a further 36 patients were found to have fibroids during the antenatal period. In 3 cases red degeneration of the fibroid occurred. Two of these cases were treated conservatively in this hospital, while the third case was admitted to the surgical unit of a local hospital and had myomectomy performed at laparotomy for acute abdominal pain. In 2 cases only did the fibroids offer any obstruction to delivery; in both cases there was a transverse lie and elective Caesarean section was performed. In this group there were 15 normal deliveries, 11 forceps deliveries, 9 Caesarean sections and 1 abortion.

In the previous medical histories, tuberculosis and heart disease were prominent, the cause of the latter being, in all cases, rheumatic carditis. Three of the patients showed evidence of decompensation before conception. All 3 survived. Four patients had active pulmonary tuberculosis. The age of this group of patients accounts for the number of cases of hypertension and carcinoma. The discovery of 5 cases of syphilis shows the value of routine first-visit serological tests on all patients. The other 6 cases of syphilis referred to in Table III had already been diagnosed.

TABLE III
Past History

Gynaecological		Medical	
Infertility D. and C.	20	Heart disease	17
Insufflation	6	Hypertension	5
Dysmenorrhoea D and C.	12	Duodenal ulcer	6
Menorrhagia D. and C.	3	Tuberculosis	14
Ovarian cyst	9	Myxoedema	2
Erosion	4	Thyrotoxicosis	2
Suspension	2	Syphilis	11
Cervical polyp	2	Epilepsy	2
Imperforate hymen	1	Nephritis	2
Double uterus	1	Carcinoma	3
Myomectomy	11	Anaemia, Pernicious	2
Dyspareunia	1	Iron deficiency	3

Pre-eclamptic toxaemia and hypertension were present in no less than 217 cases—an incidence of 36·5 per cent. As many of the patients were not seen until late in pregnancy, it is difficult to differentiate between pre-eclamptic toxaemia and hypertension with or without superimposed toxaemia. The incidence of these complications is undoubtedly higher than in other published series but the overall incidence of toxaemia in the hospital was 18·1 per cent. This high incidence is partly explained by the selection of cases for admission and the large number of emergencies accepted. In the series under review, 50 of the 99 emergency admissions suffered from pre-eclamptic toxaemia, a patient being so classified when the blood pressure was 140/90 mm. Hg or over, and there was proteinuria or oedema present. It will be seen later how this complication influenced the method of delivery.

Four patients developed eclamptic fits in the antenatal period. It is regrettable to have to admit that 3 of these patients were booked for confinement and were attending the hospital antenatal clinic. Two of the 4 patients were delivered by forceps, one by Caesarean section and one had a normal delivery. One of the patients had two further fits after delivery. These patients indicate that the antenatal care of any elderly primigravida must be more rigorous than for her younger sister.

Nephritis was not a complication in any patient and hyperemesis occurred in 5 patients but did not present any serious difficulty.

Six cases of placenta praevia—an incidence of 1·1 per cent—and 23 cases of other types of ante-partum haemorrhage—an incidence of 3·9 per cent—were found in the series. The overall incidence in the hospital was 1·5 per cent and 3·6 per cent respectively. It has been stated that the incidence of ante-partum haemorrhage is increased in the elderly primigravida (Waters and Wager, 1950). No conclusion, however, can be drawn from these figures, as a large number of cases of ante-partum haemorrhage are usually referred to this hospital for admission, therefore the figures do not represent the true incidence of the condition.

Placenta praevia, type I, was present in 3 of the cases and types II, III and IV in 1 case each. In the other group of ante-partum haemorrhages there were 11 cases of non-toxic haemorrhage and 4 cases where the haemorrhage was due to a cervical polypus. In a further 4 cases the cause was unknown.

All authors agree that there is a high incidence of malpresentation and mal-position, and this was the case in this series. Miller (1931) found the incidence of persistent occipito-posterior position to be 36·5 per cent and of breech presentation to be 12 per cent. Table IV shows the numbers and incidence in this series. It is quite possible that the incidence of mal-position of the vertex was higher because in the majority of cases delivered by Caesarean section the position of the head was not recorded. It was noted that in a large number of patients, rupture of the membranes was the first sign that labour was about to commence. This is probably related to the high incidence of mal-position of the head. Dennen and Ainslie (1951) recorded rupture of the membranes before the onset of labour in 20 per cent of their cases.

Labour was allowed to start in 532 cases, and

TABLE IV

Abnormal Presentation

Presentation	No.	Percentage	Method of Delivery
Breech	34	5·7	13 assisted; 12 Caesarean sections; 9 extractions
Shoulder	3	0·5	Caesarean section
Face	2	0·3	1 Caesarean section; 1 normal
Brow	2	0·3	1 Caesarean section; 1 internal cephalic version and forceps
Deep transverse arrest ..	73	12·3	66 forceps; 7 Caesarean sections
Persistent occipito-posterior	44	7·4	26 forceps (2 face to pubes); 15 Caesarean sections; 3 spontaneously face to pubes

TABLE V
Duration of Labour

Hours	No.	Percentage
0–6	61	11·5
7–12	150	28·2
13–24	180	33·8
25–48	112	21·0
48+	29	5·5

its duration for these is set out in Table V. In only 29 patients did labour exceed 48 hours. The average duration was 20 hours. Twin pregnancy was associated with a much longer labour, the average duration in the series being 38 hours. The average figure for all primigravidae in the hospital was 16½ hours.

Labour was induced surgically in 58 cases. Pre-eclamptic toxaemia was the usual indication (34 cases), followed by accidental haemorrhage (12 cases). Artificial rupture of the membranes was performed in 54 cases and a stomach tube inserted in 4 cases. In several cases labour failed to start and as the condition of the patient deteriorated recourse was made to delivery by Caesarean section.

Delivery was spontaneous in only 235 cases (39·5 per cent). Forceps delivery was performed in 236 cases (39·6 per cent) and Caesarean section in 124 cases (20·9 per cent). The forceps rate in the hospital was 16·3 per cent and the Caesarean section rate 8 per cent. The indications for forceps delivery and Caesarean section are shown in Tables VI and VII. In 90 cases it was necessary to rotate the head from the occipito-posterior position or the occipito-transverse position before forceps were applied.

TABLE VI
Indications for Forceps Delivery

Delay in 2nd stage	142
Foetal distress	62
Maternal distress	20
Premature baby	3
Eclamptic fit	1
Accidental haemorrhage in labour	2
Twins (4 sets both twins; 2 sets only the first)	6
Total	236

TABLE VII
Indications for Caesarean Section

Pre-eclamptic toxaemia and hypertension (elective)	22
Failed induction for above	10
Trial of labour	40
Disproportion (elective)	13
Accidental haemorrhage	3
Placenta praevia	2
Foetal distress early in labour	12
Breech presentation	12
Shoulder presentation	3
Face presentation	1
Brow presentation	1
Prolapsed cord	2
Diabetes	2
Eclamptic fit	1
Total	124

In 2 cases this was impossible and the infants were delivered in the occipito-posterior position.

As a general rule, the third stage was normal. Post-partum haemorrhage occurred in 23 cases. In 10 of these the placenta had already been expelled. Manual removal of the placenta was performed in 44 cases, an incidence of 9·3 per cent. The overall hospital incidence is 3·4 per cent. However, in many cases it was recorded as a prophylactic measure as the patients were already under an anaesthetic. Intravenous ergometrine is not used as a routine during delivery. Thus, the high rate of forceps deliveries accounts in part for the high rate of manual removal of the placenta. Nixon had an incidence of 8·3 per cent. He described the procedure as the most dangerous of obstetrical operations, while in this series it was often performed prophylactically!

Among the total of 612 infants delivered there were 39 stillbirths and 20 neonatal deaths. This is an uncorrected stillbirth rate of 6·4 per cent and neonatal death rate of 3·3 per cent. The overall hospital figures are 5 per cent and 2·7 per cent—also uncorrected. There were 14 intrauterine deaths before admission. If these and the 6 abnormal foetuses are deducted the stillbirth rate was only 3·2 per cent.

Nine abnormal infants were delivered—6 were monsters, including 2 anencephalics and 2 hydrocephalics—all were stillborn. One infant

TABLE VIII

Complications in Puerperium

Pyrexia		84
Urinary	57	
Genital	15	
Chest	9	
Breast abscess	2	
Unknown	1	
Thrombophlebitis		23
Superficial	19	
Deep	3	
Pelvic	1	
Secondary post-partum haemorrhage		8
Wound infection		24
Anuria		1
Confusional psychosis		1
Eclamptic fits		1
Referred for surgery		15

had a minor deformity of both ears. The other 2 infants were mongols and both survived.

The complications during the puerperium are recorded in Table VIII. The morbidity rate has not been recorded; instead, all cases of pyrexia requiring treatment are recorded. One patient who had a very severe accidental haemorrhage suffered from anuria; recovery occurred after treatment by the regime described by Bull, Bywaters and Joekes (1950).

Fifteen patients were referred to the gynaecological department: for treatment of stress incontinence (6), prolapse (2), ovarian cysts (2), cervical erosion (2), pelvic abscess (1), vesico-vaginal fistula (1) and vaginal cyst (1).

The only maternal death occurred in 1947, a period when all primigravidae with non-engagement of the head at 38 weeks were admitted for pelvic assessment under anaesthesia. This patient was admitted for this examination which was performed under chloroform anaesthesia. She came into labour 2 days later and a very difficult forceps delivery was performed after a labour lasting 48 hours. She died 3 days afterwards from acute yellow atrophy of the liver.

DISCUSSION

The percentage of elderly primigravidae in the total hospital admissions varies from hospital to hospital. Posner and Luftman (1952) reported 0·4 per cent while Denman and Ainslie (1951) reported 4·2 per cent. The number of cases reviewed also varied from 88 (Miller, 1931) to 649 (Waters and Wager, 1950).

The variations can be accounted for by racial and economic conditions and by the age adopted by the author for his définition of "elderly primigravida". In India the incidence of elderly primigravidae is very low and Dutta (1948) claimed that a woman pregnant for the first time after 26 years of age must be so classed. Most American authors note the low incidence among American negroes. In the present series it was noticed that the incidence has been less during the past few years. In the period 1947–1951 the incidence was 4·1 per cent while in the period 1952–1956 the incidence was only 2·9 per cent.

It has been stated by Nixon (1931) and Waters and Wager (1950) that the abortion rate is high (10 per cent), and is three times that of the young primigravida. It is suggested that the presence of fibroids may account for this. This has not been confirmed by this series; of the 47 patients with fibroids only 3 aborted. The abortion rate cannot be verified as only a limited number of abortions are admitted to the hospital. On the other hand, the incidence of fibroids was quite low (7·5 per cent) as compared with 16·9 per cent of Randall and Taylor (1949).

It is agreed by all authors that the incidence of pre-eclamptic toxaemia and hypertension in the elderly primigravida is high and is usually twice that of the hospital figure. The incidences in the present series are 36·5 per cent and 18·1 per cent. Weisl (1953), however, records incidences of 4·7 per cent and 2·2 per cent.

Strict antenatal care is necessary in the management of these patients and visits should be made to the clinic more often than usual. It is suggested that every patient should be seen at weekly intervals from the 30th week. At the first sign of developing toxaemia she should be admitted to hospital and only in exceptional circumstances should she be allowed home before delivery, even if the toxaemia has responded to treatment.

Thompson (1951) states that artificial rupture of the membranes is unsuitable as a method of induction in these cases on account of the increased foetal risks and recommends delivery by

elective Caesarean section as early as the 34th week. In this hospital, however, a more conservative approach is adopted. Artificial rupture of the membranes was carried out in 34 patients with toxaemia. Ten of these were subsequently delivered by Caesarean section because the toxaemia worsened and labour had not commenced. In addition, 22 other patients with toxaemia were delivered by elective Caesarean section.

Pre-eclamptic toxaemia thus accounted for just over 25 per cent of the patients delivered by Caesarean section. It is believed that this high figure can be reduced by the combination of artificial rupture of the membranes and the pitocin drip which is a more recent method of induction.

Routine X-ray pelvimetry and examination under anaesthesia of all primigravidae, in whom the head is not engaged at the 38th week, has not been practised for several years. It has been found that vaginal examination after 12 hours in labour is a more accurate guide to the ultimate outcome. Many unnecessary anaesthetics are therefore avoided.

Prophylactic forceps delivery was rarely performed on account of the patient's age, and in over 30 per cent of vaginal deliveries the second stage exceeded 2 hours. Only when there was an obstetrical indication was recourse to forceps delivery made. However, the commonest indication was delay in the second stage.

The indications for Caesarean section in these patients are less restricted than in the younger age groups. Thus, the presence of several minor complications may cause the attendant to favour Caesarean section as the safest method of delivery, e.g., a patient with a free head and who is past her estimated date of confinement may be delivered by an elective Caesarean section while a younger patient would have a trial of labour. Forty patients delivered by Caesarean section had been given a trial of labour. It was difficult to decide in many of the cases to what extent uterine "inertia" was responsible for the failure of the trial, but the impression gained was that it did not play a major part in the decisions to terminate labour.

The perinatal death rate was low. In view of the large number of patients with complications the figure is good. Miller (1931) had a stillbirth rate of 26 per cent, a large number of them being due to intracranial haemorrhage following forceps delivery. Posner and Luftman (1952) had a perinatal death rate of 14·1 per cent.

Mongolism is stated to be high among infants of elderly patients. Weisl (1953) reported an incidence of 1·08 per cent among his patients as compared with an incidence of 0·14 per cent in the hospital. In this series, the incidence was only 0·35 per cent among the elderly primigravidae.

Breast feeding was encouraged. Most patients did so while in hospital but the number who continued to do so after discharge could not be accurately ascertained. Only a small number of patients attended the postnatal clinic and among these less than 40 per cent were continuing to breast feed.

Dutta (1948) divides the elderly primigravida into two types—(*a*) the patient who married young and only conceived after many years of marriage, and (*b*) the patient who married late in life and conceived almost immediately. The difference in the groups was reflected in the type of labour and the method of delivery. In the first group the labour was long and instrumental delivery common, while in the second group labour was rapid and normal delivery usual.

This view is not held universally (Waters and Wager, 1950; and Posner and Luftman, 1952). In both articles, the writers note that in individual cases the length of marriage may influence the method of treatment but that the relationship is not sufficiently constant to be of any significance. They also point out that they have not encountered dystocia due to rigidity of the perineal tissues or inflexibility of the pelvic ligaments in those patients married a long time. Posner and Luftman (1952) also claim that the age of the patient is of no importance.

An attempt is made to show from this series that relative infertility plays no part in the method of delivery but that the age of the patient has more significance.

The patients were divided into two groups—(*a*) those married less than five years, and (*b*) those married more than five years.

Table IX shows that there is little difference in the methods of delivery and that actually those

TABLE IX

Married Less Than 5 Years			Married More Than 5 Years		
Method	No.	Per Cent	Method	No.	Per Cent
Normal delivery	149	39·0	Normal delivery	70	41·2
Forceps delivery	164	42·9	Forceps delivery	60	35·3
Caesarean section ..	69	18·1	Caesarean section	40	23·6

(In 43 cases the number of years married had not been recorded.)

TABLE X

Less Than 40 Years			More Than 40 Years		
Method	No.	Per Cent	Method	No.	Per Cent
Normal delivery	194	41·7	Normal delivery	41	31·8
Forceps delivery	191	40·9	Forceps delivery	45	34·9
Caesarean section ..	81	17·4	Caesarean section	43	33·3

TABLE XI

Under 40 Years

Married Less Than 5 Years (298 Cases)			Married More Than 5 Years (130 Cases)		
Method	No.	Per Cent	Method	No.	Per Cent
Normal delivery	120	40·3	Normal delivery	60	46·2
Forceps delivery	132	44·3	Forceps delivery	46	35·4
Caesarean section ..	46	15·4	Caesarean section	24	18·5

Over 40 Years

Married Less Than 5 Years (84 Cases)			Married More Than 5 Years (40 Cases)		
Method	No.	Per Cent	Method	No.	Per Cent
Normal delivery	29	34·5	Normal delivery	10	25·0
Forceps delivery	32	38·1	Forceps delivery	14	35·0
Caesarean section ..	23	27·4	Caesarean section	16	40·0

married over 5 years had more normal deliveries. The patients were then divided into another two groups by age—(*a*) those under 40 years, and (*b*) those over 40 years (Table X). It will be seen that the operative interference rate is much higher in those over 40 years. The Caesarean section rate, which is four times that of the hospital, is almost twice that of the younger age group.

The patients in both age groups are further sub-divided into those married less than 5 years and those married more than 5 years. These figures are shown in Table XI. In the age group under 40 years, the method of delivery was

almost the same in both groups. However, in those patients over 40 years the operative interference rate was very high—75 per cent. The number of patients in this group is small; however, 2 out of every 5 were delivered by Caesarean section.

Summary and Conclusions

(1) The definition of "elderly primigravida" is discussed. It is here defined as a primigravida aged 35 years and over.

(2) The case histories of 595 such patients admitted to the Royal Maternity Hospital in the 10-year period 1947–1956 have been reviewed.

(3) Pre-eclamptic toxaemia is a very common complication in the antenatal period. No reason was found why the incidence is so high in this hospital other than by the selection of cases for admission.

(4) The methods of delivery are discussed and the indications for operative interference tabulated. This high rate of 60·5 per cent is fully justified by the results—a maternal mortality of 0·2 per cent and a perinatal mortality of 8·9 per cent.

(5) The duration of labour is slightly increased.

(6) Foetal abnormality was not common.

(7) The patients were divided into groups by the number of years married and by their ages. The age of the patient appears to have more influence on the method of delivery than does the number of years married.

(8) The patient can be re-assured that a normal pregnancy is expected and her infant will be normal, but that she requires closer supervision than a younger patient.

(9) The practitioner should be warned to watch for early signs of toxaemia and to treat them seriously.

(10) The high operative delivery rate, which, though justified, means that ideally all elderly primigravidae should be delivered in hospital.

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A COMMENT ON MALIGNANT DISEASE IN CHILDREN FOLLOWING INTRA-UTERINE IRRADIATION

BY

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A PRELIMINARY report by Stewart and Giles (1956) suggested the possibility of induction of leukaemia following intra-uterine irradiation. A later and more comprehensive investigation by Stewart and others (1958) modified the earlier findings without diminishing anxiety.

These articles prompted this present investigation, the purpose of which was to find out how often malignant disease in the child followed intra-uterine X-radiation, although not necessarily caused by it.

At Cresswell Maternity Hospital, Dumfries, X-ray pelvimetry has been carried out as a routine procedure in primigravidae and in all parous patients where the obstetric history does not exclude a possibility of pelvic contraction. Between 1945 and 1956 5,070 pelvimetry X-rays were performed. In the earlier years, 1945 to 1951, three views were taken, brim, lateral and outlet and, thereafter, due to a national shortage of film stocks, pelvimetry investigations were limited to a single lateral view and, only if the measurements thus obtained were diminished, were further views carried out. This enquiry was carried out in the following three ways:

(1) The mothers who had left the hospital with their children alive and well were sent a simple form of enquiry.

(2) The Medical Officers of Health for Dumfries, Kircudbright and Wigtown were asked for the names of children who had died of malignant disease since 1945 and these names were checked for a record of X-ray pelvimetry during that particular pregnancy.

(3) Local medical practitioners were questioned as to whether they had had any case of malignant disease in children in their practice; if so, retrospective search was made in the records to discover if radiation had been carried out in the mother.

RESULTS

(1) Of the 5,070 deliveries resulting in 5,089 children born (twins, 19) 172 children were stillborn and 92 died during the neonatal period.

TABLE I
Causes of Perinatal Mortality

Stillbirths		Neonatal Deaths	
Congenital abnormalities	30	Congenital abnormalities	17
Accidental haemorrhage	20	Prematurity	46
Birth trauma	9	Intracranial haemorrhage	12
Prolapsed cord	8	Atelectasis	13
Cerebral haemorrhage	6	Infection	3
Infection	1	Erythroblastosis	1
Prematurity	7		
Erythroblastosis	1		
Causes unknown	90		
Total	172	Total	92

Table I shows the causes of death. The 4,806 mothers who left the hospital with their children alive and well were asked to complete a form of enquiry into the child's health, any illnesses, hospital attendances and, if the child had died, the name of the doctor attending the child during the last illness. To avoid any possible domestic upset the children of 65 unmarried mothers were investigated by the lady almoner.

Two thousand eight hundred and sixty-nine children were traced, 1,002 letters were returned "address unknown" and the remainder did not reply.

Twenty-six children and 5 mothers had died. Table II records the causes of death of the children.

TABLE II

Previous Irradiation of Mother
Causes of Death

Children	
1. Orbital neuroblastoma.	10. Multiple congenital abnormality.
2. Reticulum sarcoma.	11. Coeliac disease.
3. Leukaemia.	12. Pyloric disease.
4. "Leukaemia."	13. Road accidents (2 cases).
5. Bronchopneumonia (6).	14. Air crash.
6. Gastroenteritis (3).	15. Tetanus.
7. Meningitis.	16. Suffocated by bedclothes.
8. Virus pneumonia.	
9. Congenital heart disease.	

One case was certified as dying from "leukaemia" in Table II. There was no haematological or post-mortem examination of the child who was seen by the certifying practitioner after death. Therefore, the cause of death should be grouped as "unknown".

(2) Children who had died of malignant disease in Dumfries, Kircudbright and Wigtown since 1945 totalled 14, all under 10 years. One child in Dumfries-shire, still alive, suffers from chronic myeloid leukaemia.

There is no record of any of these mothers having been X-rayed during the particular pregnancy when the child subsequently developed or died of malignant disease.

(3) In December, 1958, a male child aged 8 years was admitted to Dumfries Infirmary suffering from acute leukaemia. The mother had been X-rayed for pelvimetry during her pregnancy.

Including all children traced, stillbirths of known cause and neonatal deaths, the fate of 3,043 children is known. Three cases of malignant disease have occurred, an orbital neuroblastoma, a reticulum cell sarcoma and an acute leukaemia.

With the constant movement of the population it was impossible to trace all the children, although replies were received from such distant places as Canada, New Zealand and Africa.

It is appreciated that there may be some cases of malignancy among those who did not answer the questionnaire or those who had changed their domicile and, further, that any one of the children who were certified as dying of bronchopneumonia may, in fact, have died of leukaemia, a disease in which the terminal stages may simulate bronchopneumonia.

It is realized that a control group of the same type, i.e., primigravidae not X-rayed during pregnancy, is necessary for comparison with the group under review. Furthermore, any one of these children from that portion of the group X-rayed in the later years of the series may develop malignant disease in the next few years.

Nevertheless, the review would appear to indicate the extreme rarity of malignant conditions in the first five years of life. It has been suggested by Lewis (1958) that, if the preliminary deductions of Stewart were correct, one possible "X-ray induced" leukaemia may occur in every 40,000 deliveries. This means that in a hospital such as Cresswell Maternity Hospital, where an average of 1,600 births takes place each year, one possible case of leukaemia induced by X-rays *may* occur every 27 years.

The oncogenic activity of X-rays has resulted in several hypotheses. X-rays are known to damage the genes of the cell nucleus and the enzyme hypothesis proposes that certain "gene dependent" enzymes are depressed or the enzymes are altered to produce abnormal cells.

The virus hypothesis claims to account for the vertical transmission of tumours through generations of carriers eventually being triggered by factors such as X-rays or chemical poisons (Gross, 1958).

Geneticists have studied the effect of ionizing radiation on the broad bean (*Vicia faba*) and in the Drosophila Fly and maintain that an increase of this radiation augments the rate of mutation in the genes. As well as the possible oncogenic effects of X-rays are there more mutants in the present generation?—a question which cannot be answered until many decades have passed.

The amount of radiation received by the patient during X-ray pelvimetry is small. A

recent survey carried out under the direction of Dr. J. M. A. Lenihan of the Regional Physics Laboratory, Glasgow, has shown that the dosage received by patients at Cresswell Maternity Hospital is as follows:

Lateral View	0·1–2 r.
Brim View	0·7 r.
Suprapubic Angle View	0·3 r.

Williams (1943) reported that brim and lateral views subject the patient to 0·47 r. Parlee (1958) observed for the lateral films 0·9 r.

In this hospital great care is taken to reduce the radiation dosage by increase of the patient-tube distance, the use of filters and cones and reducing to a minimum the numbers of exposures necessary to achieve a satisfactory film by employing only specially trained technical staff for this purpose.

Against the damage of radiation must be balanced the advantages of accurate pelvic measurements and the possible but immeasurable saving of life by the early detection of pelvic abnormalities.

The superiority of X-ray pelvimetry over clinical pelvimetry should be obvious following the comparisons between the two methods which have been reported (Walshe, 1940; Kenny, 1944).

Conclusions

Following X-ray pelvimetry in 3,043 cases, 3 children developed malignant disease. Whether or not the exposure of the patient to X-rays was the cause of any of these tumours is not known, but the chance of malignancy being produced by X-ray pelvimetry is so small that X-ray is justifiable in essential cases.

Acknowledgments

I am grateful to Dr. J. Bruce Dewar for his assistance in this investigation and to our Secretarial Staff who dealt with the voluminous postbag.

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UTERO-ADNEXAL INFARCTION

Report of a Case

BY

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AND

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UTERO-ADNEXAL infarction is a somewhat uncommon complication of criminal abortion. The condition has been described in detail by Elstub (1956).

The aetiology is uniform. The introduction of a noxious fluid *per vaginam* such that it passes through the cervix, into the decidua and into or behind the implantation site of the developing placenta, results in a high concentration of this fluid passing outwards in the enlarged uterine veins, thus causing venous gangrene of the tissues drained by the veins so involved. In this case the fundus of the uterus, the tubes and ovaries and the infundibulo-pelvic ligaments were distended and engorged with thrombosed venous blood (Figs. 1 and 2). The fluid appears to have passed upward behind the developing embryo and entered the enlarged veins towards the fundus of the uterus resulting in a peripheral spread outwards along the tubes and infundibulo-pelvic ligaments.

The clinical picture is also fairly uniform. The patient presents as an acute abdominal emergency associated with an abortion. Port wine urine and renal failure are frequent associated findings.

The treatment is surgical and to combat the anuria which frequently develops after operation Bull's regime should be commenced immediately. In this case it was necessary to refer the patient for dialysis by means of the artificial kidney.

CASE REPORT

Mrs. M.F. Aged 27 years. Para-5. M.C.5/28. Blood group A, Rhesus negative.

This patient was admitted to the Gynaecological Ward at Eastern District Hospital as an inevitable abortion at 10 p.m. on 4th December, 1957. On admission she was suffering from severe abdominal pain causing orthopnoea. Her pulse rate was 80 per minute and her blood pressure was 160/100 millimetres of mercury.

The abdomen was distended and tympanytic, very rigid and extremely tender on palpation. Bowel sounds were absent. No clinical localizing signs were present. The patient's respiratory difficulty was due to sharp pain on inspiration localized to the right hypochondrium and left clavicular region. Clinical examination of her chest revealed no abnormality. Straight X-rays of chest and abdomen were negative.

Vaginal examination showed the cervix to be one-finger dilated. A 10-weeks size foetus was lying in the vagina and was noted to be in two pieces. A minimal amount of vaginal haemorrhage was present. There was no significant odour from the vaginal discharge. Pelvic and abdominal tenderness was too severe to allow any detailed examination. Rectal examination revealed acute tenderness in the pelvis but no other abnormality could be detected.

A specimen of urine was noted to be port wine in colour. A catheter specimen was obtained. Microscopic examination showed a few pus cells but no red blood cells. Albumin was present. Guaiac test for blood pigment was positive. Ehrlich's test for porphobilinogen was negative. (Spectroscopic examination of the urine the following day proved the pigment to be oxyhaemoglobin.)

FIG. 1
Uterus and appendages showing massive infarction.

FIG. 2
Section of uterus showing areas of massive infarction.

The patient was in great distress from the abdominal pain and dyspnoea and in considerable mental anguish. The history she gave on admission was misleading and quite untrue as was discovered later. Apart from the fact that she had no previous operations or serious illnesses, and that she had been perfectly well until the day of admission, no further useful information could be obtained to help in making the diagnosis. She emphatically denied any possibility of criminal interference with her pregnancy which, incidentally, she claimed not to know about.

An acute abdominal emergency was obviously present. Acute porphyria was excluded by the negative Ehrlich test. The possibility of some complication resulting from a criminal abortion was very much in mind. Four hours after admission her pulse rate was 160 per minute and her blood pressure 130/80 millimetres of mercury. With the patient's condition thus deteriorating, laparotomy was undertaken at 2 p.m. on 5th December, 1957.

A blood transfusion was commenced and the patient anaesthetized with cyclopropane and flaxadine. The abdomen was opened by a right para median incision. Blood-stained free fluid was present in the peritoneal cavity. Massive infarction of the uterus, tubes and ovaries was noted with extensive thrombosis and ecchymosis extending up to the common iliac veins and along the infundibulo-pelvic ligaments and ovarian vessels some way up the posterior abdominal wall. A ragged circular laceration was present in the posterior fornix and was considered to be a perforation probably due to interference from below. Total hysterectomy and bilateral salpingo-oöphorectomy was performed with some difficulty owing to the oozing, oedema and friability of the tissues and the abdomen closed without drainage.

The morning after operation the patient gave true account of her condition. Her last normal period commenced on 15th August, 1957 and was followed by vaginal bleeding on 12th September, 1957 for two days, and on 4th October, 1957 for one day. She considered herself to be pregnant.

Just after midnight on 4th December, 1957 she mixed about half a bar of carbolic soap in one pint of warm water, and douched herself vigorously with a Higginson's syringe which she inserted as far into her vagina as possible.

At 1 a.m. she began to experience suprapubic abdominal pain. At 5 a.m. she noticed her urine to be blood-stained. At 10 a.m. vaginal bleeding commenced. The abdominal pain increased steadily in severity and by 6 p.m. she was in great distress with pain in her right hypochondrium and left shoulder. She then called her doctor who arranged her admission to hospital with the diagnosis of an inevitable abortion.

Further tests on the urine were as follows:

Total uroporphyrins — nil detected.
Total coproporphyrins — less than 1·5 micrograms/24 hours.
Test for carbol in urine — negative with ferric chloride.

Post-operatively the patient was immediately commenced on a modified Bull's Regime in view of the haemoglobinuria and almost certain renal damage. She received two pints of blood at operation. Thereafter she had a Ryle's tube passed and for the next four days her total daily intake was 1,000 ml. of 40 per cent glucose by intra-gastric drip. Her blood electrolytes and urine output are charted on Table I.

TABLE I

	5/12/57	6/12/57	7/12/57	8/12/57	9/12/57	14/1/58	18/1/58
Blood urea in mg./100 ml. ..	180	225	—	290	345	26	31
Serum sodium in m.eq./l.	154	152	—	131	128	136	142
Sodium potassium in m.eq./l. ..	5·2	4·9	—	5·2	7·2	4·7	4·7
True plasma chloride in m.eq./l. ..	95·5	95·7	—	92·5	88	103	108·8
Alkali reserve in m.eq./l.	21·4	21·0	—	20·4	17·3	24·6	32
Daily urinary output in ounces ..	9	5½	5¾	5¾	3½	—	—

Penicillin and Streptomycin were administered for the first two days and Aureomycin for the 3rd, 4th and 5th post-operative days.

The patient's general condition improved but her renal function did not recover and her electrolyte picture became critical. On 9th December, 1957 she was transferred to the Metabolic Disturbances in Surgery Research Unit at Leeds General Infirmary so that she could obtain the assistance of the artificial kidney.

The patient was successfully treated at Leeds and returned to the Eastern District Hospital on 13th January, 1958. The following is an extract from the report sent by Dr. Parsons from Leeds:

"Mrs. F. arrived on 10.12.57. We decided to dialyse her immediately and finished a six-hour dialysis at 9.33 p.m. No untoward occurrences occurred during the dialysis. The next day we observed a very marked and unusually rapid clinical improvement. She was taking an interest in her surroundings, was quite rational, all her vomiting had ceased and indeed she was complaining of hunger. She took her allotted quota of glucose water and vitamins by mouth with no difficulty. Four days later the urine output started to return and on the following day we were able to give her a litre of milk daily. Forty-eight hours later her condition had improved so much that she was able to take a low protein diet. Thereafter she made uninterrupted progress, the renal function improved day by day and the blood chemistry returned to relatively normal values. The only complication that we encountered was the abdominal wound. We removed the stitches on 18.12.57 and the wound at that time looked very healthy, but within four hours it had broken down and a large abscess beneath started to discharge. I seem to remember giving some warning about the frequency of this occurrence in anuric patients, and it was no surprise to me that the wound completely disrupted on Christmas Day, and had to be resutured. At this time the surgeon noted quite a marked pelvic inflammatory reaction and we treated her with a full course of chloromycetin (in view of bacteriological reports) and shortwave diathermy."

The patient's condition was excellent on her return from Leeds. Her wound which had been resutured was granulating satisfactorily. Her recovery continued. She was ambulant and her wound almost completely healed when she was allowed home on 3rd February, 1958. Further electrolyte studies are noted on Table I.

She reported to the follow-up clinic on 12th March, 1958 and was very well. There was no vaginal discharge or urinary upset. Her abdomen was well healed. Vaginal examination showed the vault to be firm and healed and the pelvis clear.

Summary

(1) A case of utero-adnexal infarction is described.

(2) The aetiology, diagnosis, and treatment of the condition are detailed.

(3) The diagnosis can be made on the combination of the following clinical signs:

(*a*) Acute abdominal emergency.
(*b*) Abortion.
(*c*) Port wine urine.
(*d*) Anuria.

We wish to express our appreciation of the immense assistance given in this case by the Metabolic Disturbances in Surgery Research Unit of Leeds General Infirmary. The patient was transferred there on an intensely cold and foggy night and she undoubtedly owes her life to the prompt attention which she received at the hands of Dr. Parsons and his team on arrival.

We are also indebted to Mr. Hugh Stirling, Consultant Gynaecologist, Eastern District Hospital, Glasgow, for permission to publish this case.

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RECURRENT ERYSIPELAS FOLLOWING VULVECTOMY

BY

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RECURRENT erysipelas is a clinical entity well recognized by dermatologists. It may involve the nose, ears and—in some cases of lymphatic disorder—the legs and arms may show recurrent infection. On the other hand, erysipelas of the vulval area seems to be rare. Way (1951) saw erysipelas following vulvectomy in 3 cases. He stated that the lesions were usually confined to the wound area and the legs. Although an alarmingly high temperature accompanied the disease there was a rapid response to adequate doses of sulphonamides and the condition had never proved serious. In 1 of his 3 cases the patient had 3 attacks of the disease, the last attack being 6 years after operation.

We have seen 2 cases of recurrent erysipelas following vulvectomy and feel that these are worthy of record.

Case 1. Miss A. Age 39

This patient was seen by Mr. R. Watson in July, 1949, with a hard nodule 3 cm. in diameter, arising from the inner aspect of the right labium major, surrounded by leukoplakia of the rest of the vulva. A few days later a local vulvectomy with wide excision of the tumour was performed. The histological report indicated that the nodular lesion was, in fact, a well-differentiated squamous celled carcinoma, and consequently a bilateral inguinal lymphadenectomy was later carried out. Histological examination of the glands revealed elements of a well-differentiated keratinizing squamous celled carcinoma. The patient's convalescence was uneventful and a vaginal swab obtained no growth of pathogenic organisms.

In September, 1950, the patient developed a febrile illness with erysipelas-like swelling localized to the region of the inguinal scars. Though the attack was very severe it soon responded to sulphonamide therapy. However, further attacks occurred and she was first seen by one of us (R.B.C.) in October, 1950, when a third attack of erysipelas was diagnosed. The typical erysipelas plaque formation was seen around both inguinal scars and also spreading postero-laterally towards the buttocks. It rapidly responded to a course of systemic penicillin. One month later a violent relapse occurred with a very similar clinical appearance and culture of a vaginal swab taken on re-admission to hospital obtained a growth of *Streptococcus haemolyticus*. The lesion again responded to penicillin but 3 days after discharge from hospital another similar attack of erysipelas developed. Again *Str. haemolyticus* was cultured from the vaginal swab and the question of a possible focus of streptococcal infection in the pelvis was considered. Accordingly a pelvic examination was carried out under anaesthesia. No pelvic disease was found apart from marked stenosis of the vaginal introitus, possibly causing inadequate drainage and accounting for the recurrent vaginal infection. The introitus was therefore

dilated. Penicillin therapy was also given but relapse again occurred as soon as treatment was stopped. A course of chlortetracycline was tried but recurrence occurred as soon as the treatment ceased.

Finally the decision was made to maintain the patient on continuous oral penicillin 200,000 units, three times a day. The lesion fully resolved and did not recur thereafter.

Two years later, in 1953, the penicillin tablets were stopped and a further series of erysipelas attacks, identical to the previous ones, appeared. Accordingly continuous oral penicillin was re-instituted and again the attacks stopped.

Eight years after her original operation the patient remains fit and well provided she still continues with the oral penicillin therapy.

Case 2. Mrs. B. Age 75

This elderly lady was seen by one of us (L.M.N.) in July, 1958, complaining of an ulcer of the vulva for six weeks. On examination the lesion appeared to be a carcinomatous ulcer 4 cm. in diameter, on the left labium majus and associated with a very tender and swollen left inguinal gland. The patient was febrile and as she had failed to respond to a course of penicillin given prior to her admission, a course of streptomycin was prescribed and combined with local treatment to the vulva and groin. This produced a satisfactory resolution of the inguinal adenitis and accordingly on 31st July, 1958, a radical vulvectomy with bilateral inguinal lymphadenectomy was carried out. Histological examination confirmed a well-differentiated squamous celled carcinoma with bilateral involvement of the inguinal glands, and culture of the inflamed inguinal gland obtained a pure growth of *Str. haemolyticus*.

The patient's convalescence was most satisfactory until the 23rd day after operation, when she became ill with a marked pyrexia and an erysipelas plaque appeared in the right groin, around the lateral half of the wound, but extending down the leg for 10 cm., and also postero-laterally towards the buttocks. Swabs taken of the wound site on this and subsequent occasions showed no evidence of *Str. haemolyticus*, though *Proteus vulgaris* and *Staphylococcus aureus* were isolated.

The erysipelas responded well to a course of systemic penicillin. Two days after this was stopped, however, a sudden and violent relapse took place with complete repetition of the above clinical picture. The patient was given a further 6 days penicillin but again 1 day after stopping this treatment a third and even more severe attack occurred. It was then decided to give the patient continuous oral penicillin, 400,000 units, twice daily. The patient has continued on this regime and no further attacks of erysipelas have occurred up to the present.

Unfortunately secondary carcinomatous deposits developed in the vulval region and have been confirmed by biopsy. Some of the secondaries were fixed to the pubic bones and it was therefore decided that further radical treatment was impracticable.

Comment

We consider these two cases interesting because they both showed recurrent erysipelas which, although it involved the lateral aspects of the inguinal wounds, tended to spread postero-laterally over the buttocks following the course of lymphatics. Both cases responded well to continuous oral penicillin, and relapse occurred with remarkable rapidity on withdrawal of the penicillin. Neither patient seemed to develop any immunity to the *Str. haemolyticus* and, indeed, the attacks occurring after withdrawal of the penicillin seemed to increase in severity rather than the reverse.

Summary

Two cases of recurrent erysipelas following vulvectomy with bilateral inguinal lymphadenectomy for carcinoma of the vulva are described. Both cases required continuous oral penicillin therapy before the attacks were controlled.

Acknowledgments

We are grateful to Mr. R. Watson for permission to publish these cases and for his help and advice, and also to Dr. W. E. Bryan for his histological reports.

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VASA PRAEVIA IN TWIN PREGNANCY

Report of Two Cases

BY

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VASA praevia has been defined as a condition in which foetal blood vessels, unsupported by either umbilical cord or placental tissue, traverse the foetal membranes in relation to the lower uterine segment in front of the presenting part (Evans, 1952). Occasionally these vessels run between the main placenta and a succenturiate lobe or between the two halves of a bipartite placenta; more commonly there is a velamentous insertion of the cord associated with a low-lying placenta. Velamentous insertion is nine times more frequent in multiple than single pregnancies (Eastman, 1956) and placenta praevia is also relatively common with twins; that vasa praevia would complicate twin pregnancy might, therefore, be expected. In fact only four well-documented cases have been found in the accessible literature and all these were associated with uniovular twins.

One case was reported in 1896, by Knapp of Prague who appears not to have found an earlier record in an extensive study of relevant literature. Three further publications are of more recent date (Kobak and Cohen, 1939; Records, 1940; Groseclose, 1951). Two additional cases are recorded here.

Case 1

Mrs. C., aged 34 years, gravida-3, attended the antenatal clinic at the Birmingham Maternity Hospital on 17th December, 1954, when 35-weeks pregnant. Her 2 previous pregnancies had resulted in normal deliveries of healthy single infants. The last confinement had taken place about 4 years earlier. She had been referred because of her large girth and proved to have twins, presenting by the vertex and by the breech respectively. The patient was, therefore, booked for hospital confinement. Three weeks later she was admitted for rest because her blood pressure had risen to 132/90 and oedema of both lower limbs was evident. No further signs of toxaemia developed. Labour commenced spontaneously two days before term with both infants now presenting by the vertex. The first stage lasted just over 4 hours. Both foetal hearts were beating regularly until about 15 minutes before full dilatation of the cervix; then the heart sounds of one twin were recorded as 120 per minute and irregular and those of the other twin were 140 per minute and regular. This result was confirmed 10 minutes later.

Almost immediately after full dilatation the head of the first infant presented at the vulva, with the membranes still intact. Rupture of the forewaters released clear fluid but delivery of the infant was followed by discharge of heavily blood-stained liquor. The baby, a boy weighing 5 pounds 13 ounces, was unusually pale and gasped once only; all efforts at resuscitation were unsuccessful.

Meanwhile the membranes of the second twin had ruptured spontaneously and the baby was delivered normally 15 minutes after the first. The liquor was clear but a blood loss of some 10 ounces followed immediately after delivery. This baby—also a male—weighing 7 pounds 4 ounces, was soon breathing normally and appeared to be in excellent condition. The third stage of labour was completed without complications. Mother and surviving twin were in due course discharged from hospital.

The placenta was of monochorionic diamniotic type and weighed 2 pounds 4 ounces. The

first twin's umbilical cord had a velamentous insertion and one of the large unsupported vessels was torn across (Fig. 1). This portion of the placenta was very pale (Fig. 2), in contrast to the second twin's portion which looked rather congested; in the latter the cord was inserted in close relation to the amniotic septum. No obvious circulatory anastomoses between the two parts of the placenta were visible.

Post-mortem examination of the first twin confirmed the general pallor; the internal organs were markedly anaemic. There was no evidence of any developmental anomaly. The lungs were unexpanded. No petechiae or haemorrhages were noticed on any of the serous membranes or elsewhere. The mesenteric lymph nodes were visibly enlarged.

Histological findings agreed with the naked eye appearances. Of interest is the microscopic picture of the liver (Fig. 3); extra-medullary haemopoiesis is marked but not to the extent usually found in erythroblastosis foetalis; intracellular glycogen is abundant, consistent with sudden death soon after birth before the glycogen stores of the liver could be used up. In the lungs there is distension of the alveolar system by amniotic fluid, but no evidence of aeration. The lymph nodes show evidence of extra-medullary haemopoiesis.

Case 2

Mrs. A., a primigravida, aged 27, was admitted to the City General Hospital, Stoke-on-Trent, as an emergency on 18th March, 1957, when 35-weeks pregnant, because of an ante-partum haemorrhage. The loss had been painless and had ceased on admission. The patient's general condition was good. A clinical diagnosis of twins both presenting by the vertex was made and the two foetal hearts were audible and regular. The presenting head was free above the pelvic brim. Since there was no evidence of toxaemic accidental haemorrhage, placenta praevia was diagnosed and a conservative regime commenced.

Five days later there was a further small vaginal haemorrhage followed after several hours by a heavier loss which continued. The patient's condition remained good but at this stage only one foetal heart could be identified. Accordingly, immediate delivery was decided upon and a lower segment Caesarean section was performed without preliminary examination *per vaginam*. At delivery the first baby was found to be ashen white and lifeless. Its heart was not beating and it made no respiratory effort. The second baby was also extremely pale; although it gasped several times all resuscitation measures were unsuccessful. Both babies were female, weighing 4 pounds and 4 pounds 2 ounces respectively.

The placenta was praevia. It was situated on the posterior wall with the placental edge extending almost to the internal os.

The placenta weighed 1 pound 8 ounces and was unusually pale in appearance. It was monochorionic and diamniotic in type but no obvious circulatory anastomoses were visible on the surface. The cord of the first twin had a velamentous insertion 5–6 inches from the placental edge. One of the vessels traversing the membranes had ruptured 1 inch from the placenta. A small plug of thrombus blocked the point of rupture. The cord of the second twin had a normal placental insertion.

Post-mortem examination. Both infants were of less than full-term size and conspicuously pale. There was no post-mortem discoloration of the dependent parts.

The internal organs of both twins were very pale and hardly any blood was seen in the heart and great vessels. Whilst one infant showed evidence of some, though very poor, pulmonary expansion, the lungs of the other were entirely unaerated; sub-pleural petechiae indicating intra-partum anoxia were seen in both cases.

Discussion

Vasa praevia is a comparatively rare condition and is exceedingly dangerous to the foetus. The danger lies not only in exsanguination from ruptured foetal vessels but also in pressure on the velamentous vessels by the presenting part with resultant foetal asphyxia. Torrey (1952) gives a perinatal mortality of 60 per cent in vasa praevia and this rate is increased to 73 per cent when the vessels actually rupture.

Clinically one can rarely distinguish ante-partum haemorrhage due to ruptured vasa praevia from that attributable to other causes. Greenhill (1956) advised that suspicions should be aroused when a slight but continuous haemorrhage follows rupture of the membranes and the foetal heartrate steadily rises from this time. It is noteworthy that in both cases described above the membranes remained

FIG. 1

Case 1. Foetal aspect of the twin placenta showing the amniotic septum and the velamentous insertion of one cord; one of the umbilical vessels here is lacerated.

FIG. 2

Case 1. Decidual surface of the placenta showing the pallor of the portion with velamentous insertion of the cord.

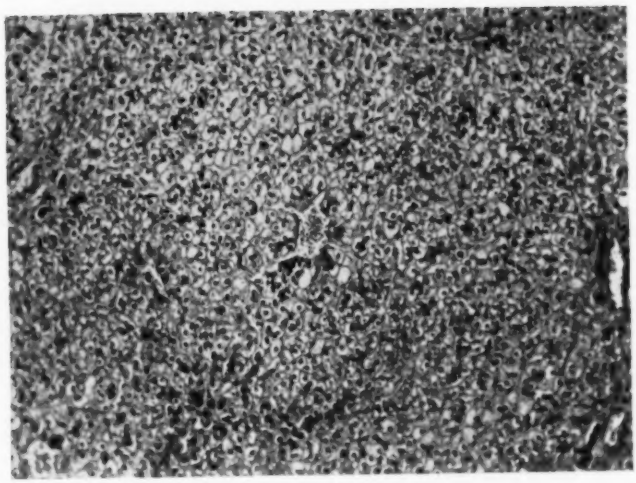

FIG. 3
Case 1. Histological picture of liver in exsanguinated infant.

intact although rupture of vasa praevia had occurred.

The fact that it is foetal blood which is shed in a rupture of vasa praevia and maternal blood in most other types of ante-partum haemorrhage can be utilized for differential diagnosis. The test described by Mitchell, Anderson and Russell (1957) provides a rapid and simple method of recognizing a significant level of foetal haemoglobin in a sample of blood; if it could be used in all cases of ante-partum haemorrhage the occasional case of ruptured vasa might be detected before exsanguination had occurred. In most cases of ante-partum haemorrhage, however, it is impossible to obtain sufficient suitable blood from the vagina to carry out the test adequately.

Rupture of vasa praevia not only imperils the directly affected infant, but the second twin is also in danger of exsanguination through the anastomotic vessels of the "third circulation" of the placenta (Schatz, 1884). In the 6 recorded cases (including 2 described here) all sets of twins were uniovular but both babies were lost in only two instances. In the other four cases the second twin was healthy and apparently not suffering from blood loss. From this it may be deduced either that the second twin was delivered before any significant blood had been lost through the placental anastomoses or else that in some uniovular twin placentae the anastomoses are too small to matter. When an exsanguinated first twin is delivered it would seem wise to proceed with the delivery of the second twin by the quickest appropriate method.

Summary

Two cases of rupture of vasa praevia in twin pregnancy are described. In each instance the placenta was of monochorionic diamniotic type indicating uniovular twinning. In the first case the directly affected infant died from exsanguination, his twin brother survived. In the second case both infants were lost. The total number of cases recorded is raised to six.

Acknowledgments

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AN UNUSUAL CASE OF CHORIOCARCINOMA AND A CONSIDERATION OF THE VASCULAR LESION

BY

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NUMEROUS cases of choriocarcinoma have been reported including recent series by Park and Lees (1950) and Hou and Pang (1956). It was felt however that the present case should be reported because of certain unusual features.

A sixteen year old girl presented clinically as a case of cerebral haemorrhage. No history of pregnancy was obtained and the gross appearances at autopsy were not suggestive of choriocarcinoma, no obvious primary tumour or metastasis being found. Nevertheless the study of serial sections of a vessel from the site of the haemorrhage showed trophoblastic cells infiltrating the vessel wall. A careful search then revealed a few trophoblastic cells in the myometrium and lung. These cells, like those infiltrating the cerebral vessel were presumably malignant, yet chorionic villi, presumptive evidence of a benign process, were demonstrated in a pulmonary artery.

HISTORY

The patient was well until one year ago but since then she has suffered from severe headaches. On the day before admission, while on her way home from school, she complained of a sudden severe pain in the right side of the head. A diagnosis of cerebral haemorrhage was made by the family doctor and she was admitted to a medical ward of this hospital.*

Systematic Enquiry

Cough for past month. *Family history:* no hypertension.

On Examination

Fairly well nourished afebrile semicomatose girl lying curled up in bed. Mucosa of fair colour. No lymphadenopathy.

Central nervous system. Responds to painful stimuli, neck rigidity +, Kernigs +. Cranial nerves: (R) facial palsy. Pupils: circular, equal, central, just reacting to light.

	R	L	
Limbs: Tone—reduced resistive			
Reflexes	+	+	brisk especially in lower limbs.
Plantars:	↑	↑	

Abdominal: none elicited.

Cardiovascular system: No signs of congestive failure. B.P. 100/60. Pulse 60/min. regular. *Apex:* not displaced. Heart sounds normal.

Chest: clear.

Abdomen: no abnormality was noted.

Investigations

Hb. 11·6 g. per cent. W.B.C. 11,100 per c.mm. V.D.R.L. negative. Lumbar puncture—fluid uniformly blood stained in all specimens.

Pressure: 160 mm., free rise to 280 mm. and fall.

Cells, 90. *Protein*, 150 mg.

Lange: Zone ii (tabetic) curve.

Progress: During the first three days her mental condition improved. She answered simple questions and was able to take food. However, from the fourth day her condition steadily deteriorated and she died on the ninth day after admission.

* University College Hospital, Jamaica.

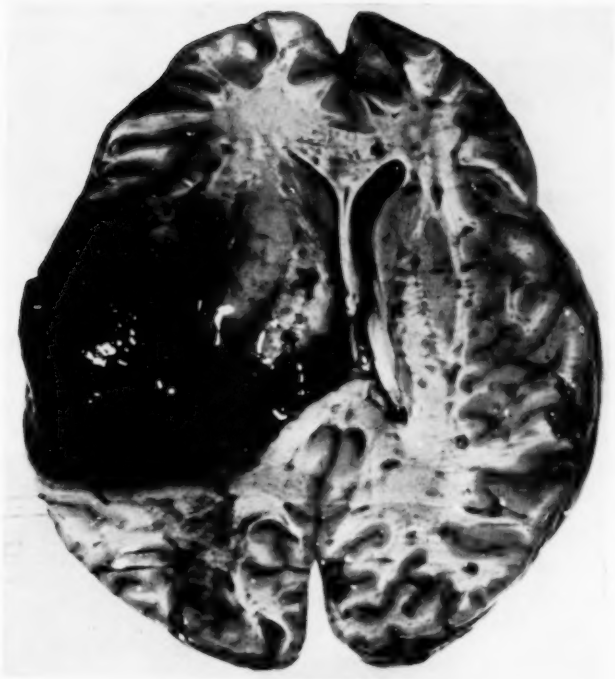

FIG. 1
Massive haemorrhage into the left cerebral hemisphere.

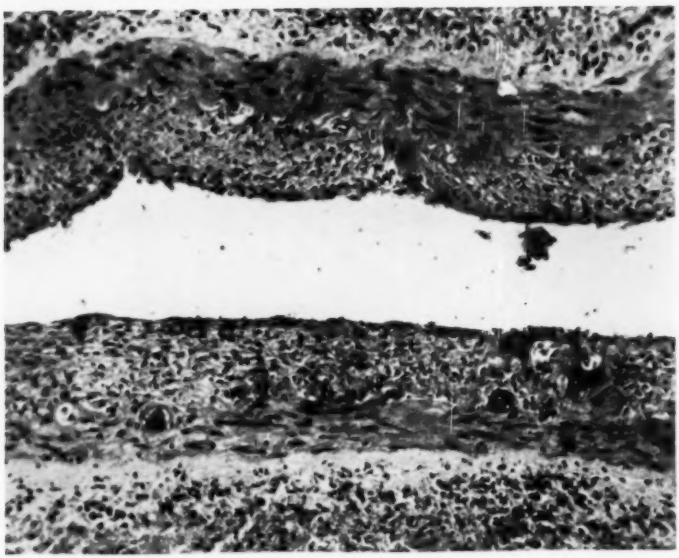

FIG. 2

Cerebral artery infiltrated by trophoblastic cells and showing intimal thickening, muscle necrosis and perivascular infiltrations of inflammatory cells. H. & E. ×99.

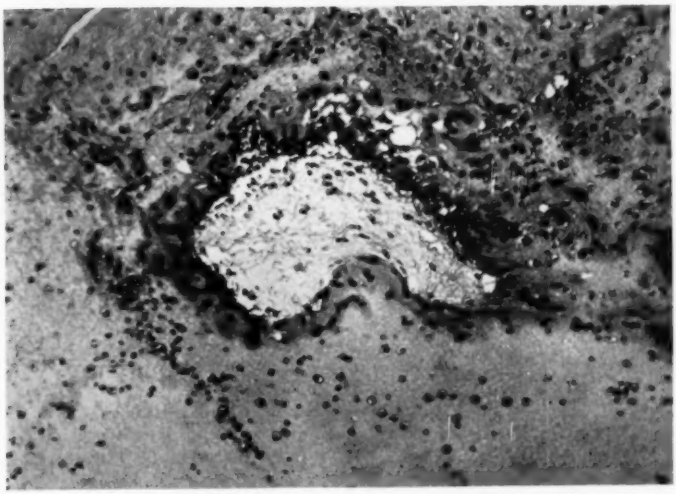

FIG. 3

Chorionic villus in the lumen of a pulmonary artery. H. & E. ×90.

Summary of Relevant Autopsy Findings

The subject was a young but fully developed female showing no remarkable external appearance.

Lungs: The left weighed 316 g. and the right 330 g. All the lobes of both lungs were congested. Four firm foci were palpated in the lower lobes. These were interpreted as bronchopneumonic.

Reproductive organs: The hymen was perforate. No abnormality was noted in the vagina. The uterus was normal in size and external appearances and no remarkable feature was seen when it was sectioned. A cystic corpus luteum measuring 2·5 cm. in diameter was found in the right ovary. The left ovary was normal.

Brain: There was a large haemorrhage into the left cerebral hemisphere (Fig. 1). This had destroyed the brain tissue between the ventricle and the cortical surface and had leaked into the subdural space. The vessels were dissected out but showed no gross abnormality. No tumour was visible.

No remarkable feature was noted in the heart, liver, spleen, kidneys, bladder, gastro-intestinal tract, pancreas, adrenals or thyroid.

Relevant Histological Findings

Brain: In addition to haemorrhage there was a small cerebral softening with lipoid filled macrophages. The haemorrhage surrounded a small artery which showed periarterial infiltrations of chronic inflammatory cells; degeneration and fibrinoid necrosis of the muscle; destruction and fragmentation of the elastica; and intimal thickening (Fig. 2). Trophoblastic cells were seen in the thickened intima and in the muscle coats. In the intima they were frequently flattened and difficult to recognize and in the muscle they were associated with necrosis. The meninges were thickened and infiltrated by inflammatory cells.

Lung: (left) rather degenerate chorionic villi were seen in the lumen of one pulmonary artery (Fig. 3), and trophoblastic cells and blood clot in another.

Uterus: Trophoblastic cells were seen infiltrating the myometrium but there was no haemorrhage or necrosis. The endometrium was little more than fibrous stroma and no epithelium was seen.

Right ovary: This showed a cystic corpus luteum.

Discussion

The brain is a common site for metastatic choriocarcinoma and cerebral haemorrhage is frequently encountered. In many instances, to judge from the literature, the real nature of the condition is not suspected and experience in the present case suggests that unexplained cerebral haemorrhage may sometimes be due to microscopic and therefore undetected metastatic choriocarcinoma.

Hou and Pang (1956) attribute the haemorrhage to rupture of the cerebral metastasis. No discrete cerebral metastasis was found in the case described here but the study of serial sections of a vessel from the site of the haemorrhage revealed an arteritis, with necrosis of the wall in the immediate vicinity of trophoblastic cells. These changes, which probably resulted in rupture of the vessel, may well have been due to the proteolytic activity of the trophoblast as described by Friedheim (1929). An interesting feature in this vessel was the presence of intimal thickening. It is possible that this represents the incorporation into the wall, in the manner described by Duguid (1946), of blood clot which was part of a metastasis once occupying the lumen.

Acosta-Sison (1957) believes that only some chorioepithelial cells are malignant and that these may co-exist with a normal pregnancy. A similar speculation must apply to the present case in which "deported" chorionic villi were found in the presence of malignant trophoblast although it is likely that a mole rather than a normal pregnancy was concerned.

It is generally held that villi are not found in choriocarcinoma. They are however a feature of chorioadenoma destruens, a lesion, associated with a mole, invariably benign and showing usually nothing more than the invasion of the myometrium by one or more villi. Although it may, according to Hertig and Mansell (1956), be associated with local pelvic metastases of

trophoblast. It would seem therefore that the present case falls somewhere between chorioadenoma destruens and choriocarcinoma, but nearer the latter than the former.

Summary

An unusual case presenting as a cerebral haemorrhage in a 16-year old girl and showing features of both choriocarcinoma and chorioadenoma destruens is described.

It is suggested that some unexplained cases of cerebral haemorrhage may be due to microscopic and therefore undetected metastatic choriocarcinoma.

The vascular lesion is discussed.

Acknowledgments

I wish to thank Professor Arthur Hertig for his interest in this case and Dr. John Gourlay for reading the manuscript.

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A CLINICAL AND PATHOLOGICAL STUDY OF ADENOACANTHOMA OF THE UTERINE BODY*

BY

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THIS paper deals with the clinical and pathological behaviour of 42 cases of adenoacanthomata observed over a period of 8 years at The Royal Women's Hospital, Melbourne.

Adenoacanthoma is the term given to adenocarcinomatous tumours of the uterine body in which islands of squamous epithelium occur (Willis, 1948). They are usually graded on the histological appearance of the adenocarcinomatous component, as the squamous component is frequently of well differentiated structure, often identical in histological appearance with the squamous metaplasia accompanying benign lesions. However, the extent of the squamous component varies in different tumours. There is a small group in which the squamous elements have the structure of a squamous cell carcinoma. On occasions, the adenomatous and squamous areas may be so clearly demarcated as to give the impression of two separate tumours co-existing in the uterine body.

VIEWS ON THE ORIGIN AND BEHAVIOUR OF ADENOACANTHOMA

Novak and Yui (1936) believed that the squamous component was probably derived from certain undifferentiated cells lying beneath the epithelial-stromal junction. But, since these "indifferent" cells have not been demonstrated, E. R. Novak and Nally (1957) suggest that the more likely origin is a direct transformation from the lining epithelium, less commonly from the stroma. They claim that chronic infections or hormonal influences could be a stimulus for this transformation.

There appears to be a great variation of opinion regarding the relative degree of malignancy and the tendency of these tumours to metastasize. They have been stated to be tumours of low grade malignancy. Novak and Nally (1957), in fact, claim that "the presence of acanthosis in fundal adenocarcinoma is an excellent prognostic sign and almost guarantees the absence of invasion or distant extension". Stein and Torek (1930), Beecham and Friday (1942), Postoloff and Rodenberg (1954), and others have found that adnexal or distant metastases are so rare that they have published special case reports of these occurrences. Willis (1948) does not draw a distinction between the degree of malignancy of adenoacanthoma and that of ordinary endometrial adenocarcinoma. Meigs (1934) considers that its prognosis lies midway between that of carcinoma of the cervix and carcinoma of the body of the uterus, as metastasis is more frequent and extensive than with ordinary endometrial adenocarcinoma. Way (1951) and Stander (1956), in independent analysis of secondary tumours occurring in the vagina from uterine carcinoma, found a high proportion were derived from endometrial adenoacanthoma.

Reports of the frequency of adenoacanthoma vary. Healy and Cutler (1930) and Murphy (1936) regard it as a relatively rare tumour since

* Communicated to a combined clinical meeting of the Victorian and Tasmanian State Committees of the Royal College of Obstetricians and Gynaecologists at Launceston on 28th February, 1959.

they found its incidence in their series of endometrial carcinomas to be 3 per cent and 1 per cent respectively. Nicholson (1923), Willis (1948), and Kottmeier (1953), however, have found a significantly high proportion of adenoacanthomas among endometrial carcinomas, the incidence varying from 15 to 39 per cent.

Views as to the radiosensitivity also differ. Kottmeier (1953) found that adenoacanthomata possess a fair degree of primary radiosensitivity, certainly comparable with that of endometrial adenocarcinoma. Other authors (Schattenberg and Ziskind, 1940) believe that adenoacanthoma responds poorly to radium. In fact, Ferguson in 1931 stated that no case had been reported of complete disappearance of the adenoacanthoma following application of radium.

Material Investigated in this Series

From 1950 to 1957 inclusive there were 180 patients with cancer of the uterine body admitted to The Royal Women's Hospital, and in 42 the tumour was an adenoacanthoma (24 per cent). The pathological diagnosis of adenoacanthoma was made from microscopic examination of endometrial scrapings or of the uterine contents after hysterectomy, the criterion for diagnosis being the presence of an adenocarcinomatous tumour containing islands of squamous epithelium.

Age

Adenoacanthoma was found to be chiefly a disease of the post-menopausal years, 36 out of 42 patients having reached their menopause. The youngest was aged 32 and the oldest 76, the average being 59 years. The age distribution is summarized in Table I.

Table I

Age Distribution of Adenoacanthoma

Age Groups	Number of Patients
35–45 years	4
46–55 years	12
56–65 years	14
66–75 years	10
Over 75 years	2
Average age = 59 years	

Table II

Parity

	No children	One child	More than one child
Number of patients	10	12	20

Parity

The parity tended to be low, a finding common to endometrial carcinoma in general.

Symptoms

In the post-menopausal group of patients the presenting symptom was either vaginal bleeding or blood-stained discharge. In the pre-menopausal group, intermenstrual bleeding or heavy loss with the period was present.

Mode of Treatment

Since 1950, the general method of treatment of endometrial carcinoma at the Royal Women's Hospital has been intracavitary irradiation followed by surgery. Pre-operative irradiation is not used where there are technical contra-indications. Four to 6 weeks after irradiation the patient is re-examined and, if she is considered to be a satisfactory surgical risk, a Wertheim hysterectomy and pelvic lymphadenectomy are performed. If there is doubt that the patient will tolerate such radical surgery, particularly in cases where fractional curettage suggests that the growth is confined to the fundus, or where the technical difficulties may be great as in extreme obesity, the lesser surgical procedure of total hysterectomy and bilateral salpingo-oöphorectomy is done. Irradiation alone is reserved for patients who are unfit to withstand surgery or in whom the growth is too advanced. Table III summarizes the methods of treatment.

Although this table shows an operability rate of 74 per cent the more radical operation was performed upon less than half of these patients. This illustrates the high incidence of patients who were a relatively poor surgical risk, a feature of patients with endometrial carcinoma generally.

TABLE III

Mode of Treatment

Year	Radiotherapy Alone	Panhysterectomy*	Wertheim and Lymphadenectomy*	Too Advanced for Treatment
1950	1	1	–	–
1951	2	1	2	–
1952	–	3	1	–
1953	2	1	3	–
1954	2	1	–	1
1955	–	5	–	1
1956	1	1	4	–
1957	1	3	5	–
Total	9	16	15	2

* Includes cases with pre-operative radon.

Total number of cases=42. Operability rate=74 per cent.

Percentage of surgical cases subjected to "Wertheim's"=48 per cent.

TABLE IV

Comparison of Three-Year Survivals of Adenoacanthoma and Adenocarcinoma (1950–1955 inclusive)

	Adenoacanthoma	Adenocarcinoma
Number of patients	27	93
Number dead or with evidence of recurrence	11	25
Number alive and with no evidence of recurrence	16 (59 per cent)	68 (73 per cent)

Speert (1949) and Finn (1950) and others claim that the majority (over 85 per cent) of recurrences in endometrial carcinoma become manifest within 3 years of treatment. Taking this as a basis, Table IV represents an analysis of 3-year survivals of both adenoacanthoma and adenocarcinoma, irrespective of the mode of treatment.

The methods of treatment have been similar in both groups of patients. Although the number is small, it suggests that adenoacanthoma is at least not less malignant than ordinary endometrial adenocarcinoma.

THE PATHOLOGICAL FEATURES

For purposes of classification the primary tumour was graded according to the degree of glandular differentiation; Grade 1, the highly differentiated form in which glandular formations are in many ways similar to glands in the normal proliferative endometrium; Grade 2, moderately well differentiated; Grade 3, poorly differentiated, in which a glandular pattern is difficult to make out; Grade 4, anaplastic, with little or no tendency to glandular formation. This grading is somewhat comparable with Broders' method of assessing the numbers of differentiated cells. There were no Grade 3 or Grade 4 growths in this series. An attempt was made to ascertain the relation between the degree of differentiation of the adenocarcinomatous component and the occurrence of extra-uterine metastasis. Table V summarizes the findings.

These figures suggest that with lesser degrees

TABLE V

Frequency of Extra-uterine Metastasis in Relation to Degree of Differentiation

Differentiation of Adenocarcinomatous Component	Number of Patients	Number showing Extra-uterine Metastasis	Percentage
Grade 1	30	6	20
Grade 2	12	4	33

TABLE VI

The Site and Nature of Metastasis of Endometrial Adenoacanthoma

Name	Sites of Metastasis			Basis of Diagnosis
	Adnexal	Nodal	Extrapelvic	
M.McF.			Pulmonary and lower 1/3 vagina	Chest X-ray. Biopsy vaginal nodule
M.M.		Right common and internal iliac		Wertheim hysterectomy and lymphadenectomy
D.R.	Left tube and ovary		Omentum	Laparotomy and biopsy
Ma.M.		Right and left obturator		Wertheim hysterectomy and lymphadenectomy
M.H.	Right ovary			Pan-hysterectomy
L.P.			Ascites and lower 1/3 vagina	Biopsy of vaginal nodule
A.S.	Left ovary			Pan-hysterectomy
E.H.	Left ovary			Pan-hysterectomy
P.K.		External iliac and aortic group	Mediastinal glands Left chest wall	Wertheim hysterectomy and lymphadenectomy. Subsequent post-mortem
V.D.	Right tube and left ovary			Wertheim hysterectomy and lymphadenectomy

of differentiation of the adenocarcinomatous component the frequency of extra-uterine metastasis may be higher; but the histological picture in the individual case was not an accurate guide to the behaviour of the tumour. Metastasis may occur whatever the degree of differentiation.

INCIDENCE AND SITES OF EXTRA-UTERINE METASTASIS

Many authors believe adnexal and distant metastasis to be uncommon with adenoacanthoma of the uterine body. In this series, 10 out of 42 patients (24 per cent) were found to have metastasis in one or more sites outside the uterine cavity. The ovary was a common site. A summary of the nature and sites of metastasis appears in Table VI.

There has been little reference in the literature to the incidence of pelvic lymphatic node metastasis with adenoacanthoma. This may be due to the fact that the Wertheim hysterectomy and lymphadenectomy are not commonly performed for carcinoma of the uterine body. In this series the incidence of lymph node metastasis was high. There were 15 patients on whom a Wertheim hysterectomy and lymphadenectomy were performed and in 3 of these histological evidence of metastasis was found. Table VII summarizes the incidence of nodal metastasis found after lymphadenectomy for adenoacanthoma and also that for ordinary endometrial carcinoma over the same period.

TABLE VII

Incidence of Lymph Node Metastasis

	Adeno-acanthoma	Adeno-carcinoma
Number of lymphadenectomies	15	45
Number with nodal metastasis	(20 per cent)	3 (7 per cent)

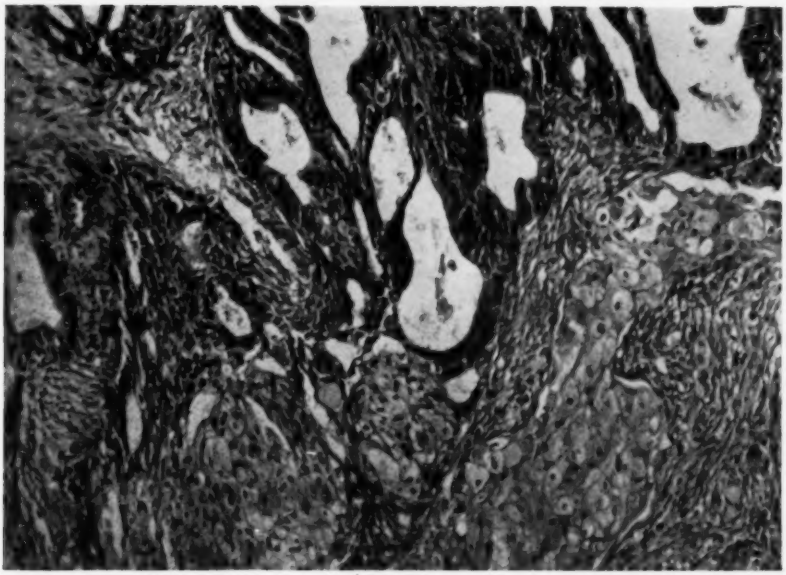

FIG. 1
Endometrial scrapings illustrating a typical adenoacanthoma of the uterine body. H. & E. ×100.

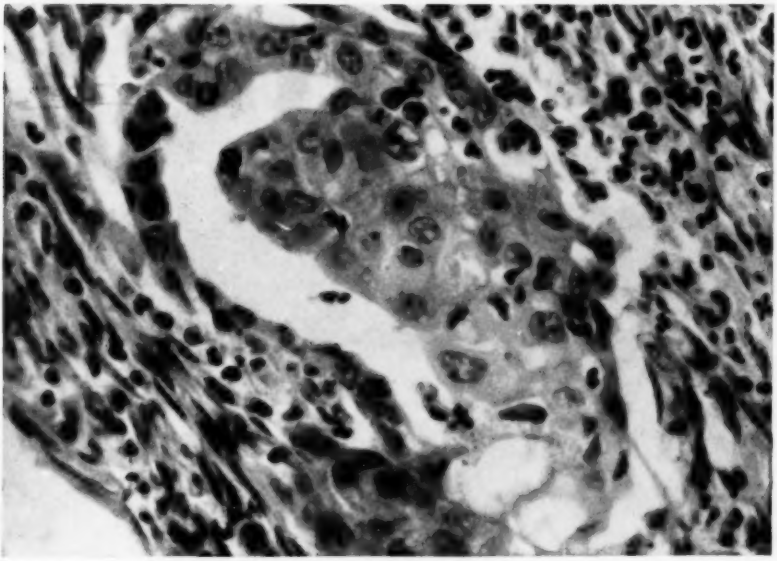

FIG. 2
A high power view of endometrial scrapings of an adenoacanthoma (patient M.M.) showing the co-existence of both squamous and adenomatous components. H. & E. ×400.

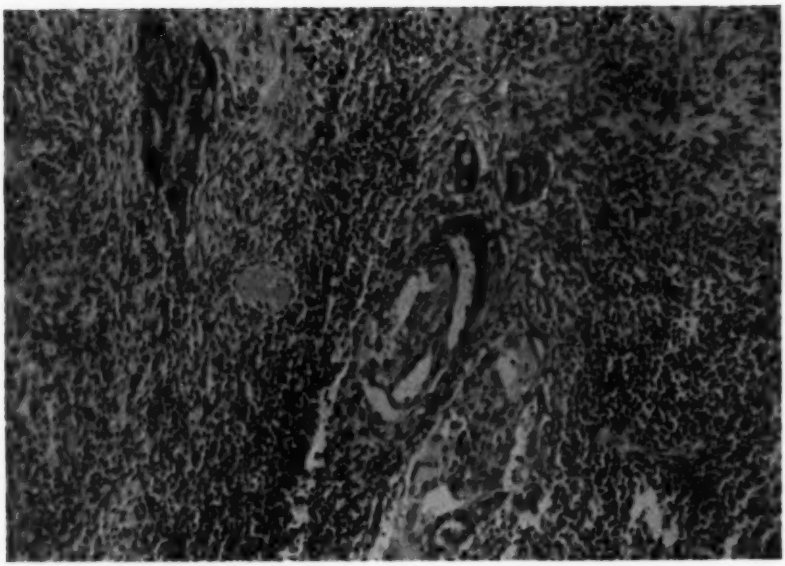

FIG. 3

Metastatic deposits in a lymph node (from same case as Fig. 2) showing adenocarcinomatous components with areas of squamous metaplasia. H. & E. ×100.

TABLE VIII

The Histological Pattern of the Primary Tumour Compared to that of the Metastasis

Patient	Site of Metastasis	Histology of Primary Tumour		Histology of Metastasis	
		Adenocarcinomatous Component	Squamous Cell Component	Adenocarcinomatous Component	Squamous Cell Component
M.McF.	Vagina (lower 1/3)	Highly differentiated (Grade 1)	Extensive, well differentiated	Highly differentiated	Extensive, well differentiated
M.M.	Common and internal iliac lymph nodes	Moderately differentiated (Grade 2)	Very extensive, well differentiated	Very little adenocarcinomatous formation	Predominantly squamous areas, well differentiated
D.R.	(*a*) Left tube and ovary (*b*) Omentum	Highly differentiated (Grade 1)	Moderate extent, well differentiated	Highly differentiated	Moderate extent, some areas well differentiated
Ma.M.	Obturator nodes	Highly differentiated (Grade 1)	Moderate extent, moderate differentiation	Very little adenocarcinomatous formation	Almost entirely composed of squamous component, well differentiated
M.H.	Right ovary	Highly differentiated (Grade 1)	Patchy, well differentiated; some areas less well differentiated	Highly differentiated	Not extensive, well differentiated
L.P.	Vagina (lower 1/3). Peritoneum	Moderately differentiated (Grade 2)	Moderate extent in parts well differentiated, in others frankly carcinomatous	Solid carcinomatous formations, with little glandular formation	Extensive, well differentiated
A.S.	Left ovary	Highly differentiated (Grade 1)	Moderate extent, well differentiated	Moderately differentiated	Extensive, well differentiated
E.H.	Left ovary	Highly differentiated (Grade 1)	Patchy areas, moderate differentiation	Highly differentiated	Patchy areas, moderate differentiation
P.K.	(*a*) External iliac nodes (*b*) Aortic nodes (*c*) Mediastinal glands (*d*) Chest wall	Moderately differentiated (Grade 2)	Extensive, highly differentiated	Moderately differentiated	No squamous formation in lymph nodes. Other sites—large areas of squamous epithelium with keratinization
V.D.	Right tube and Left ovary	Moderately differentiated (Grade 2)	Moderate extent, well differentiated; some areas extreme degree of differentiation and keratinization	Poorly differentiated	No squamous formation

The Histological Pattern of the Primary Growth Compared to that of the Metastasis

Table VIII summarizes the degree of differentiation of the glandular and squamous components in the primary tumour and its metastasis. In some, there was close similarity of structure, while in others one or other component predominated in the metastasis. Clearly, many tumours retained their inherent tendency to undergo squamous metaplasia, and in some this was almost the sole epithelial structure in the secondary site.

The Effect of Irradiation on Endometrial Adenoacanthoma

The standard method of intracavitary irradiation was the insertion of a "compound" radon tube with radioactive components differentially loaded in the tube and distributed in tandem fashion, after the manner described by Cuscaden and Oddie (1939). Table IX represents the findings after pathological examination of the operative specimens in which pre-operative irradiation was used.

Thus, there was evidence of local radiosensitivity of the adenoacanthomatous tumour in almost one-half of the cases which had pre-operative irradiation. In addition to this, two patients with histologically proven adenoacanthoma have survived for over 5 years without evidence of recurrence, their sole treatment having been intracavitary radon and deep X-ray therapy.

Table IX

The Effect of Irradiation on the Primary Growth

Number of Operative Specimens Examined After Pre-operative Radon	Number Showing No Evidence of Residual Endometrial Growth	Number with Residual Growth Present
14	6	8 (includes 2 of doubtful viability)

Discussion

This study was prompted by the disparity in the published accounts of the clinical and pathological behaviour of adenoacanthoma and that observed at The Royal Women's Hospital, Melbourne.

The age and parity of the patients and the clinical history of adenoacanthoma differed very little from those associated with ordinary endometrial carcinoma. However, in this series adenoacanthoma was not the uncommon and relatively harmless tumour some authors have claimed it to be. Almost one-quarter (24 per cent) of endometrial carcinomata presenting in a period of 8 years were adenoacanthomata, and one-quarter of these (10 out of 42 patients) developed extra-uterine metastasis despite a generally high degree of differentiation of the adenocarcinomatous element. In brief, it was impossible to gauge the likelihood of metastasis on histological appearances alone.

The sites of metastasis in these patients were varied and widespread with the ovary a common site; and the proportionate incidence of lymph node metastasis appeared appreciably higher than with ordinary endometrial carcinoma.

Another finding of interest was the considerable number of adenoacanthomata which were sensitive to radiotherapy. This again was in contrast to a common view that adenoacanthoma is a tumour which responds poorly to radium.

Why then, is there such a lack of agreement regarding the degree of malignancy of this tumour? Postoloff and Rodenberg (1954) have suggested "that the lack of widespread accepted criteria by which to make an accurate diagnosis has been responsible for this void in our knowledge". Possibly one reason why adenoacanthoma has not been given due prominence is that unless the pathologist has a particular interest in it the tumour may be regarded as a minor variant of endometrial adenocarcinoma, and the association of the squamous metaplasia is not stressed.

Summary

(1) A clinical and pathological study was made of 42 patients with adenoacanthoma of the uterine body.

(2) Adenoacanthoma was not an uncommon tumour. It comprised 24 per cent of 180 endometrial carcinomata admitted to hospital in a period of 8 years.

(3) The adenocarcinomatous component of the tumour was usually well differentiated, but high differentiation did not preclude the possibility of metastasis.

(4) The degree of malignancy of adenoacanthoma was at least comparable with that of ordinary endometrial carcinoma. Extra-uterine metastasis occurred in 10 of 42 patients (24 per cent).

(5) The incidence of lymph node metastasis in patients subjected to radical surgery and lymphadenectomy (3 of 15 patients) suggests a place for this order of surgery in patients able to tolerate it.

(6) Almost half the adenoacanthomata treated with radiotherapy were radiosensitive.

(7) In this series adenoacanthoma of the uterine body was more frequent, more malignant, metastasized more readily, and was more radiosensitive than is generally believed.

Acknowledgments

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A COMPARISON OF THE PROGNOSIS OF ADENOACANTHOMA AND ADENOCARCINOMA OF THE CORPUS UTERI

BY

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IN the course of a study of vaginal metastases (Way, 1951) it became apparent to one of us that the prognosis of adenoacanthoma of the corpus uteri might not be as favourable as is generally believed. The study revealed that, amongst 65 pure adenocarcinomas of the corpus, vaginal metastases were seen 6 times whilst, amongst 15 adenoacanthomas, vaginal metastases developed in no fewer than 8 patients. Read (1956), in a personal communication, said that he considered the prognosis of adenoacanthoma to be bad, in spite of his earlier statement to the contrary (Read, 1955).

Views on the malignancy of adenoacanthoma of the corpus vary widely. At one extreme Meigs (1943) considers the malignancy to exceed that of pure adenocarcinoma, lying midway between that of carcinoma of the corpus and that of carcinoma of the cervix. At the other extreme are Novak and Nalley (1957) who state that the presence of acanthosis in fundal adenocarcinoma is an excellent prognostic sign and almost guarantees absence of invasion or distant metastases. Most British writers such as Browne (1955) follow the latter view. American authors usually quote the Novaks' (1958) statement that squamous metaplasia is most often seen in adenocarcinoma of lesser degrees of malignancy and that these tumours have yielded relatively favourable results from a therapeutic standpoint.

The literature contains records of few series of cases sufficiently large to form any accurate opinion on prognosis. Skinner and McDonald (1940) described 7 cases of adenoacanthoma of the corpus of whom 6 survived for more than 5 years after treatment. Miller (1940) treated 23 cases of whom 16 (70 per cent) were surviving after an unstated period. More recently Novak and Nalley (1957) have described 16 cases of adenoacanthoma, in only one of which was there any evidence of myometrial invasion or distant metastases. Their patients have not yet been followed for 5 years, but the prognosis is assumed to be excellent.

MATERIAL AND METHOD

The material consists of all cases of carcinoma of the corpus uteri seen by one of us (S.W.) during the years 1940–1953 inclusive. It comprises a total of 156 patients in all of whom the diagnosis was proven histologically. Cases of carcinosarcoma and pure squamous carcinoma of the endometrium have been excluded.

The histological diagnosis of adenoacanthoma is based on the presence of well-marked squamous elements within a definite glandular carcinoma of the endometrium.

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TABLE I

Overall Results of Treatment

	Adenoacanthoma	Adenocarcinoma
Total number of cases seen	32	124*
Total number of cases treated	29	110
Number alive after 5 years	8	60
Absolute 5-year survival rate (per cent)	25	50
Relative 5-year survival rate (per cent)	27·6	54·5
5-year survival rate of "early" cases (per cent)	42·8	69·1
5-year survival rate of "late" cases (per cent)	0	13·8

* Two patients were not traced and have been excluded from the series.

The follow-up of surviving patients is for a minimum period of 5 years with the exception of 2 cases who emigrated soon after treatment, have not been traced, and are excluded from the series.

The form of treatment is classified simply as surgical or radiotherapeutic. The surgical group includes all cases in which surgery was aimed at cure, whether or not radiotherapy was also used. Radiotherapy was by intracavitary radium in almost all instances.

The stage of the disease when first seen is described as "early" or "late". Cases are classed as "early" when the growth is limited to the corpus uteri irrespective of its size. Spread outside the corpus to the cervix, peritoneum, vagina or elsewhere places the growth in the "late" group.

RESULTS

Incidence of Adenoacanthoma

Thirty-two cases of adenoacanthoma were found in a total of 156 cases of carcinoma of the corpus uteri, an incidence of 20 per cent.

Results of Treatment

Table I compares the overall results of treatment of adenocarcinoma with those of adenoacanthoma. The relative 5-year survival rate for adenocarcinoma is 54·5 per cent and for adenoacanthoma is 27·6 per cent.

Tables II and III show that the difference in prognosis, apparent in the overall results, remains when cases are separated into "early" and "late" groups. These tables also show that the usually accepted view that surgery produces better results than radiotherapy in the treatment of adenocarcinoma of the corpus also holds good for adenoacanthoma.

DISCUSSION

The series of cases described is consecutive and unselected. The form of treatment used has not been influenced by the type of tumour found. A comparison of the results of treatment of adenoacanthoma with that of adenocarcinoma is therefore valid.

It will be seen from Tables II and III that in both "early" and "late" groups, whether

TABLE II

Results of Treatment of "Early" Cases

	Adenoacanthoma		Adenocarcinoma	
	Surgery	Radiotherapy	Surgery	Radiotherapy
Number of "early" cases	16	5	67	14
Number alive after 5 years	8	1	49	7
5-year survival rate (per cent)	50	20	73	50

TABLE III
Results of Treatment of "Late" Cases

	Adenoacanthoma		Adenocarcinoma	
	Surgery	Radiotherapy	Surgery	Radiotherapy
Number of "late" cases	5	3	14	15
Number alive after 5 years	0	0	3	1
5-year survival rate (per cent)	0	0	21·4	6·7

treated by surgery or radiotherapy, the 5-year survival rate is considerably lower for adenoacanthoma than for adenocarcinoma. Although none of these differences is statistically significant, due mainly to the small size of the adenoacanthoma groups, it is obvious that the malignancy of adenoacanthoma at least equals that of adenocarcinoma. The results tend to confirm Meigs' opinion that the malignancy of adenoacanthoma lies midway between that of adenocarcinoma of the corpus and carcinoma of the cervix. These findings stand in strong contrast to the opinions of authors such as Skinner and McDonald (1940), Novak and Nalley (1957) and Novak and Novak (1958).

It is significant that in 15 of Novak and Nalley's 16 cases neither myometrial invasion nor metastases was found whereas in our series invasion was present in all cases with one exception and metastases had occurred in one-third of patients when first seen. This suggests some difference in the method of selection but, as Novak and Nalley do not describe a similarly selected group of cases of adenocarcinoma, comparison is difficult.

Novak and Nalley explain the difference in behaviour between their 16th case and the other 15 as being due to the fact that this case was in fact an "adenoepithelioma", that is to say a double strain tumour, both strains being malignant, whereas the other 15 cases were "adenoacanthomas", that is to say adenocarcinomas with areas of benign squamous metaplasia.

Whilst we admit that such may be the case, we are unable to find evidence to support this. In a review of recent cases we have seen at least one example of the squamous elements looking histologically "benign" except for the fact that these benign-looking elements were deep in the stroma, were seen in lymphatics, and were also present in a lymph node, showing clearly that they were anything but benign.

It is our opinion that much further work needs to be carried out before this aspect of the problem can be adequately answered but we feel that most cases, in the past at any rate, showing squamous elements in any form in association with an adenocarcinoma would be reported as adenoacanthoma and from this series we believe that there is no evidence to suggest that these tumours are less malignant than pure adenocarcinomas. Indeed, there is much evidence to suggest that they are more malignant.

SUMMARY

(1) The results of treatment of 32 cases of adenoacanthoma and 124 cases of adenocarcinoma of the corpus uteri are compared.

(2) The results show that the malignancy of adenoacanthoma is equal to and possibly exceeds that of adenocarcinoma without acanthosis.

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THE EFFECT OF A CHOLINE DEFICIENT DIET IN YOUNG PREGNANT RATS

BY

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PREVIOUS reports from this laboratory have been concerned with the incidence and character of the renal lesions in male weanling rats (Moore, 1957) and in female weanling rats (Moore, 1959). Neither in these reports nor in the literature, as far as the author is aware, is there data on the effect of such an experimental diet on the pregnant animal.

In the weanling rat, the renal lesions due to choline deficiency include cortical necrosis. Since a very similar renal condition may occur in human kidneys, particularly in association with obstetrical accidental haemorrhage (Sheehan and Moore, 1952) it was thought worthwhile to try and produce renal cortical necrosis in the pregnant rat by feeding a choline deficient diet.

The results show that when young pregnant rats are given such a diet renal necrosis does not occur although there is evidence that the pregnant state increases the demand for choline. In addition most animals can maintain pregnancy and achieve normal delivery whilst on the test diet. It is of interest, however, that in a few animals intra-uterine death of the foetus occurs.

METHODS AND MATERIAL

Pregnant rats of the Albino Wistar strain and weighing about 130 g. at mating were used throughout. The choline deficient diet is that fully described before (Moore, 1957). Matings were carried out with males of the same strain for a period of one week. Afterwards the females were housed singly. Three were fed the test diet for the last 16 days of pregnancy, 3 for 21 days of pregnancy and 3 for a period of about a week before conception and during the whole of pregnancy, a total feeding period of about 32 days.

A further 5 pregnant rats were fed the test diet, but with 0·5 g. per cent added choline chloride; 1 received this diet for the last 16 days of pregnancy, 2 for 21 days and 2 for a total period of about 32 days including a week prior to mating.

The effect of such test feeding in non-pregnant females of the same weight was determined on 15 animals; 5 on the test diet alone and 10 on the test diet plus choline chloride.

The delivered animals were killed either immediately post-partum or within 2 days of delivery. Others were killed at the end of the prescribed feeding period. Routine histological methods were used on the tissues. The foetuses which were delivered normally were examined histologically in 3 of the test animals and in 2 of the control animals.

RESULTS

In the *non-pregnant* animals no obvious change followed the test feeding. On histological examination a minor centrilobular fatty change was found in the liver in all of them except in the one animal which had been fed the test diet for only 16 days. This lipotrope effect is, of course, well known and is reviewed recently by Sebrell and Harris (1954). In 3 of the 10 non-pregnant animals on the test diet plus added choline chloride, the liver sustained a fine fatty change in the periportal region. This change is not regarded as a lipotrope effect but has been attributed either to protein deficiency or to amino acid imbalance (Best *et al.*, 1955).

No renal lesions were found in any group apart from a minor fatty change in some of the proximal tubules in the deep cortex.

In the *pregnant* animals test feeding for 21 days and about 32 days produced the typical severe centrilobular fatty change of choline deficiency. Those fed for the last 16 days of pregnancy had not developed such a change at the time of death but the liver showed a fine periportal fatty change similar to that mentioned above. The kidneys were normal apart from a fatty change in the proximal convoluted tubules of the deep cortex.

Delivery occurred normally with normal litters in all the test animals except one. In this animal, which had been fed for about 32 days, the foetuses resorbed without ill effects on the mother. Delivery with normal litters occurred in 3 of the control animals receiving a choline deficient diet plus added choline, but in the 2 which had received the diet for about 32 days, the foetuses resorbed. The foetuses which were delivered normally were also histologically normal.

Discussion

Within the limits of the experiments, choline deficiency does not produce renal damage in pregnant rats. It may be argued that the duration of the feeding periods was not long enough. However, in other experiments in this laboratory (unpublished) it was found impossible to ensure conception or maintain pregnancy when choline deficient diets had been given for, say, 54 days prior to the 7-day mating period. The test diet, although containing at least 21 per cent protein, is deficient in, at least, the sulphur containing amino acids and this factor of amino acid imbalance may be responsible for the breeding failures.

It is of interest in this connexion that Nelson and Evans (1953) found that rats would not mate if fed a protein deficient diet and that even if mating did occur there was a failure of implantation.

The suggestion of a qualitative protein deficiency may also explain the resorption of foetuses which occurred in 3 animals. Certainly resorption of foetuses follows if the protein is quantitatively reduced. Nelson and Evans (1953) found that a protein free diet from the day of breeding in normal rats resulted in 90 to 100 per cent resorptions, usually at the 9th or 10th day of gestation. It is of interest that this effect of protein deprivation is probably hormonally determined, for in subsequent work the same workers (1954) found that oestrone or progesterone singly or together could maintain pregnancy in such rats.

In humans there is no evidence that derangements of choline metabolism nor protein deficiency are involved in renal cortical necrosis or in accidental haemorrhage; the liver in the latter condition does not show a lipotrope effect, i.e. a fatty change (Sheehan and Moore, 1952, p. 13). Furthermore, in toxaemia which is not infrequently associated with accidental haemorrhage, Sims (1951) found that there was no significant difference in methionine and choline excretion between normal and toxaemic pregnant women. Nor did his evidence indicate that a generalized protein deficiency had any part to play in toxaemia.

Summary

A choline deficient diet does not produce renal damage in young pregnant rats. The only abnormal effect other than a lipotrope change is that the foetuses may resorb. This effect is most probably due to the protein inadequacy of the test diet; it is not a specific effect of choline deficiency.

Acknowledgment

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A CASE OF ECTOPIA CORDIS DIAGNOSED CLINICALLY *IN UTERO*

BY

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THE patient was a European woman, aged 40, gravida-2. She was first seen on the 4th December, 1955. Her last menstrual period began on the 10th October, 1955, and she complained of severe nausea and vomiting. Her weight was 116 pounds, her blood pressure 100/70 and her urine contained a trace of albumin, but no acetone, bile or sugar. Her haemoglobin was 70 per cent (Haldane), the red blood cell count 3·6 million, the Kahn test negative, her blood group was "O", Rhesus negative (her husband, group "A", Rhesus positive), there were not any abnormal antibodies.

The relevant past history was that she was delivered by forceps in 1949 of a normal male child. There were not any abnormalities. She was suspected of having a duodenal ulcer in 1953 with negative radiological findings.

She was seen again on the 11th January, 1956, still complaining of nausea and vomiting. There had been a bout of painless bleeding 14 days before which had not recurred. Nothing abnormal was found on pelvic examination and the size of the uterus corresponded with the date of her last menstruation.

On the 11th February (18th week), she complained of varicose veins of the legs and multiple spider naevi on the arms. The nausea had ceased.

She was seen at regular intervals and no abnormality was recorded until the 3rd May (29th week), when she was noted to have gained 8 pounds in weight in 1 month and there was a marked degree of hydramnios. X-ray of the uterus showed a single foetus without any evident abnormality. The degree of hydramnios increased steadily. Her blood was re-examined for abnormal antibodies on the 22nd June and none was found.

Because of the increasing distress caused by the greatly enlarged uterus, the patient was admitted on the 26th June (37th week) for high rupture of membranes. Her total weight gain at this time was 34 pounds. The presentation was vertex and the foetal heart distantly heard because of the hydramnios. Thirty ounces of yellow-coloured liquor were drained. Contractions began 2 hours later.

Labour was carefully watched and it was noted that even with moderate contractions, the foetal heart slowed to 100 beats per minute, recovering rapidly to 140 per minute in the intervals. With strong contractions the heart could not be heard but returned strongly as the contraction died away. The foetal position was difficult to define at first but as the liquor drained away palpation became easy. During the latter part of labour, the foetal back was directly anterior, both shoulders being easily palpated, and yet the foetal heart sounds could not be heard anywhere over the back. On the other hand the sounds were heard strongly far out on each flank. Taken in conjunction with the disappearance of the heart sounds during contractions and their rapid reappearance in the intervals, this phenomenon could be explained by the heart's lying outside the body wall and a diagnosis of ectopia cordis was made.

After a labour lasting 5 hours and 35 minutes, a low forceps delivery was performed and a female child weighing 7 pounds was delivered with eventration of the heart, liver, spleen and intestines (Fig. 1).

The heart was beating strongly on delivery and peristaltic movements of the gut were active.

No attempt was made to resuscitate the child because of the gross deformity and the child did not make any spontaneous effort to breathe. In spite of this the heart continued to beat strongly for approximately 12 hours and it is suggested that sufficient oxygen diffused through the peritoneal and pericardial coverings of the ectopic viscera to supply the child's requirements.

The third stage and puerperium were normal.

SUMMARY

This is a case of an elderly gravida-2 who had vaginal bleeding in early pregnancy and subacute hydramnios beginning at 29-weeks gestation, in whom eventration of the foetal heart was diagnosed clinically in labour. The child's heart continued to beat for 12 hours after delivery in spite of the apparent absence of any respiratory exchange either spontaneous or artificial.

ACKNOWLEDGMENT

I have to record my thanks to Mr. Bennett Austin for taking the photograph, Mr. Anthony Khoo for the typing, both of the University of Malaya, and to the Director of Medical Services, Singapore, for permission to publish this case.

FIG. 1
Eventration of heart, liver, spleen and intestines.

TWIN PREGNANCY: WELL-FORMED HYDATIDIFORM MOLE ASSOCIATED WITH A NORMAL VIABLE CHILD

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TWIN pregnancy in which a well-formed hydatidiform mole is associated with a normal viable child is a rarity. A 30-year old patient was admitted to the hospital on 6th January, 1959, with labour pains and bleeding. The first day of her last menstrual period was 26th April, 1958, and her expected date of delivery was 2nd February, 1959. By these dates she was about 36 weeks advanced in pregnancy. She had borne 4 children previously; all had been full-term normal deliveries. The last delivery had occurred 4 years previously. Her present pregnancy had been uneventful except for episodes of vaginal bleeding at the 7th and 8th months. At the 7th month she had noticed slight blood-stained watery discharge which had lasted for 10 days but did not worry her unduly. At the 8th month she had another episode of moderate bleeding which lasted continuously throughout that month. She was admitted to another hospital for this complaint, kept under observation for a time and advised to report periodically. She had not suffered from excessive vomiting. The patient had slight anaemia and she had angular stomatitis—evidence of avitaminosis. Her blood pressure was normal, the urine contained no albumin, and there was no oedema. Obstetric examination showed the uterus to be about the size corresponding to 36 weeks, with the foetus presenting normally. The foetal heart was audible. The baby seemed to be relatively small.

On admission the patient was having good pains and not draining liquor. There was no vaginal bleeding. Within 2½ hours of admission the membranes ruptured and the birth of a living female child soon followed. The child looked premature and weighed 4 pounds, but was otherwise normal. It was slightly asphyxiated but soon revived. As there was slight bleeding following delivery and the placenta had not been delivered within half an hour, the uterus was compressed abdominally to determine whether separation had occurred; some blood clots escaped. The patient was given 5 per cent glucose saline intravenously. She was then given an anaesthetic for manual removal of the placenta. The uterus was unusually large, which led us to suspect the possibility that there might be another foetus. A placenta that was easily reached was removed. It was normal to look at but small in size; it weighed 1 pound. While it was being removed some vesicles escaped. The uterus was explored and another placenta that was completely replaced by well-developed vesicles was removed. This also weighed 1 pound. There was a moderate degree of bleeding, but the patient responded readily to resuscitation, and she had an uneventful puerperium. It is hoped that the case can be followed by hormonal tests at regular intervals, but it is doubtful whether the patient, who is of low intelligence, will co-operate.

Twin pregnancy in which a well-formed hydatidiform mole is associated with a normal viable child must be exceptionally rare. Another case occurred a few years ago in this hospital, but then the patient aborted at the 20th week of pregnancy, and the foetus was not viable.

References to twin pregnancy with a hydatidiform mole and a viable foetus are very few. Taylor (1957) and Rose (1952) reported cases, and Rose stated that she could only trace 2 previous cases, one reported by Favreau and Bélanger (1939) and another by Waters and Crunden (1943).

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AN UNUSUAL CAUSE OF DYSPAREUNIA

BY

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VAGINISMUS is defined as a reflex spasm of the levator ani muscles beyond the voluntary control of the patient. The treatment varies with the personality of the doctor seeing the patient, but most cases of vaginismus have normal anatomy and need lengthy psychiatric treatment. The case of dyspareunia reported here could have been easily mistaken for a true vaginismus but proved to be due to extreme levator ani hypertrophy of physical origin, and because of the patient's sensible outlook responded to simple explanation.

The patient, aged 22, was first seen 2 months after her marriage. She was apprehensive, and although she had come ostensibly for contraceptive advice it was clear that there was much more to her problem. Her past history was revealing. She had been incontinent of urine all her life and although she was less wet when lying down leaked urine before she could reach a receptacle. She had worn a pad throughout her childhood and adolescence, while being treated by various practitioners for enuresis, but when she was 18 years old she attended hospital on her own initiative. Investigation at Lincoln County Hospital under the care of Mr. G. A. Bagot Walters showed her to have a poorly secreting left kidney with its ureter opening by a tiny orifice in the left upper quadrant of the vagina about 6 cm. from the introitus. A left nephrectomy was performed. The patient made a good recovery and her incontinence was cured.

Three years later she married and after 2 months came for advice. She was extremely worried that she had also a congenital deformity of her vagina as she had been unable to allow full penetration during sexual intercourse. At the interview, apart from her anxiety, she seemed to give normal emotional responses and she had a feminine appearance. When the pelvis was examined, the external genitalia were found to be normal and the hymen, which had been ruptured during her urinary investigation, admitted two fingers with ease. As the vagina was examined the levatores ani were felt to be grossly hypertrophied and when they contracted the lumen of the vagina was reduced to a slit. Further examination, however, showed these muscles to be under the voluntary control of the patient, and they were readily relaxed. The epithelium at the junction of the middle and lower thirds of the vagina, where the levatores ani encircled it, was tense and smooth and had none of the rugosity associated with the normal adult epithelium. This band of undeveloped epithelium was ¾ inch in depth but above it the vagina seemed normal apart from a faint ridge in the left fornix, presumably the site of the ectopic ureteric opening.

I thought that the vagina was developmentally normal and that the levatores ani had hypertrophied with the patient's attempts to control the leakage of urine. For the first 18 years of her life she had used her vagina as an accessory bladder and it was not surprising that the epithelium at this level had failed to develop its normal distensibility.

The patient was given general instruction in pelvic anatomy and readily accepted my explanation of her disability. As she did not wish to conceive she was given preliminary instruction in the use of a vaginal diaphragm and was asked to spend a week exploring her own anatomy and to practise inserting a soft coiled spring diaphragm Size 50. This very small diameter was the only one which would pass her mid-vaginal stenosis. A week later the vagina had dilated sufficiently for the patient to tolerate

a coiled spring diaphragm Size 60. Two months later there was still some tenseness of the mid-vagina which prevented a larger diaphragm with a circular spring being used, and as the vagina was disproportionately long for its width an oval Matrisalus diaphragm Size 75 was fitted.

Nine months later and 11 months after her marriage the patient was seen again. The only abnormality to be felt in the vagina at first was the slight ridge in the left fornix, but the patient volunteered that sometimes during intercourse she felt the tenseness of the mid-vagina recur. While the fit of her diaphragm was being checked the vaginal wall could be felt to contract down at the original site of the stenosis, although the epithelium then showed the normal adult pattern, and the levatores ani were relaxed. I thought it probable that the intrinsic vaginal muscle had increased in thickness with the hypertrophy of the levatores ani and that the stimulation of intercourse or pelvic examination still caused it to contract in an abnormal way.

When the patient was seen in May, 1959, she had been married for nearly 3 years and her discomfort during intercourse had disappeared. Vaginal examination showed no abnormality whatsoever. The ridge of tight vaginal epithelium was no longer present, the levatores ani and vaginal muscle were normal in size and the original site of the ectopic ureteric orifice could no longer be seen or felt. It was refreshing to meet a patient who had resolved a dyspareunia due to considerable physical difficulties.

Cases of ectopic ureter opening into the vagina are rare and I was unable to find any other record of dyspareunia following this abnormality.

Summary

A case is presented of dyspareunia secondary to levator ani hypertrophy of physical origin which responded to simple explanation.

I wish to thank Mrs. R. Peers, Secretary to the North Kensington Marriage Welfare Centre, for the use of my early notes on this patient, and Mr. G. A. Bagot Walters, of the Lincoln County Hospital, for giving me details of his investigation and operation.

VAGINAL FLUID α-MANNOSIDASE

With Special Reference to Cancer of the Cervix

BY

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IN a recent paper (Lawson, 1959), the presence of the enzyme β-glucuronidase in the vaginal fluid of women of different ages with and without cancer of the cervix was discussed. The same women were also studied in regard to α-mannosidase in the vaginal fluid, and the results of this investigation are now presented.

It is reasonable to assume that β-glucuronidase may be in no way unique amongst glycosidases in its distribution and behaviour *in vivo*. Conchie, Findlay and Levvy (1956, 1957) have found, for instance, that β-N-acetyl-glucosaminidase and the recently discovered α-mannosidase in mammalian tissues respond like β-glucuronidase to steroid hormone administration. The former has also been shown to participate in the catabolism of hyaluronic acid (Linker, Meyer and Weissmann, 1955), whilst it may be that the latter plays a similar role in the metabolism of mucoids containing mannose (Conchie *et al.*, 1956, 1957; Conchie and Mann, 1957). Some observations relating to these two enzymes in cancer are reported by Conchie and Levvy (1957), in which paper a few preliminary results of vaginal fluid assays are contained. The present study of vaginal fluid α-mannosidase has been undertaken in collaboration with Dr. Levvy and Dr. Conchie, whose guidance is gratefully acknowledged.

The study of α-mannosidase has certain advantages, the chief perhaps being that the substrate employed, ρ-nitrophenyl α-mannoside, can be prepared biochemically (whereas phenolphthalein glucuronide requires biosynthesis). On the debit side, it must be recorded that the colour reaction is yellow, and vaginal fluid itself frequently has a brownish-yellow hue. This means that in the test the control tubes commonly give appreciable readings so that, particularly with specimens giving low readings, an error may be introduced. The results to date suggest that vaginal fluid α-mannosidase warrants further study, but that some modification of the present technique would be helpful. An obvious advantage would be the use of a substrate giving a different colour reaction, and it is suggested that a substituted indoxyl derivative might be preferable to ρ-nitrophenyl α-mannoside.

It is not proposed to discuss α-mannosidase in detail but simply to present the findings on the same lines as has previously been done in respect of β-glucuronidase. The biochemical technique is identical in principle, but phosphate-citrate buffer pH 4·6 replaces the acetate buffer and a violet filter, Ilford No. 601, is used in the Spekker absorptiometer. Unit activity is defined as that which liberates 1 microgram of ρ-nitrophenol in 1 hour at 37° C. (Conchie and Findlay, 1959). As with β-glucuronidase, results are expressed in terms of units per gram of vaginal fluid.

RESULTS

Women without Gynaecological Cancer

Vaginal fluid α-mannosidase activity was estimated in 177 women without gynaecological cancer, the results being shown in Table I.

TABLE I

Vaginal Fluid α-Mannosidase Activity in Women without Gynaecological Cancer

α-Mannosidase Units/gram	Pre-menopausal (121)	Post-menopausal (56)
Nil	36	3
1–1,000	34	6
1,001–2,000	19	4
2,001–3,000	9	10
3,001–4,000	9	7
4,001–8,000	8	12
8,001–10,000	4	6
10,001–	2	8

TABLE II

Vaginal Fluid α-Mannosidase Activity in Women with Cancer of the Cervix

α-Mannosidase Units/gram	Pre-menopausal (20)	Post-menopausal (22)
Nil	0	0
1–1,000	1	2
1,001–2,000	2	0
2,001–3,000	2	2
3,001–4,000	2	3
4,001–8,000	10	5
8,001–10,000	0	4
10,001–	3	6

Of the 121 pre-menopausal women, some 75 per cent gave readings below 2,000 units/gram and 90 per cent below 4,000 units/gram. In the post-menopausal group of 56 women, 23 per cent gave readings under 2,000 units/gram and 54 per cent under 4,000 units/gram; the so-called "80 per cent level" was around 8,000 units/gram, and some 15 per cent showed activity over 10,000 units/gram (whereas less than 2 per cent of the pre-menopausal women showed enzyme activity of this high order).

These observations are very similar to those applicable to β-glucuronidase, namely, that low readings are common before the menopause whereas in post-menopausal women there is a definite trend towards higher vaginal fluid enzyme levels. It is noted that no woman of any age failed to show the presence of β-glucuronidase in the vaginal fluid, whereas in 30 per cent of the pre-menopausal and in 5 per cent of the post-menopausal group no α-mannosidase could be detected. This may in part result from limitations of the method to which reference has already been made. As will be shown, negative results did not occur with the cervical cancer cases.

Women with Invasive Cancer of the Cervix

α-mannosidase studies were undertaken on 42 women with untreated invasive carcinoma of the cervix, 20 being pre-menopausal and 22 post-menopausal (Table II).

Of the 20 pre-menopausal cases, 3 gave readings under 2,000 units/gram, 4 between 2,000 and 4,000 units/gram, and 13 over 4,000 units/gram. In the control group, 3 out of 4 women give readings under 2,000 units/gram, whereas with the cancer cases 4 out of 5 show readings above this level. Whilst only about 1 in 10 of the normal women present enzyme activity above 4,000 units/gram, 2 out of 3 cancer patients do so. These findings are almost identical with those for β-glucuronidase, and again it would seem that there is some correlation between increased α-mannosidase activity in the vaginal fluid and the presence of cervical carcinoma.

In the post-menopausal group of 22 cancer patients, 2 gave readings under 2,000 units/gram, 5 between 2,000 and 4,000 units/gram, and 15 above 4,000 units/gram. The proportion with levels above 4,000 units/gram (2 out of 3) is the same as that found in pre-menopausal cervical cancer cases. Because of the wide range of values in the post-menopausal controls, no helpful dividing line can be selected, but again it is evident that high levels are commonly encountered when cancer of the cervix is present; for instance, 1 normal post-menopausal woman in 4 gives readings over 8,000 units/gram whereas very nearly 1 in 2 of the cancer patients does so.

The highest readings found in the cancer series were 15,000 units/gram in a pre-menopausal case, and just over 15,000 units/gram in a post-menopausal patient. There were 2 pre-menopausal controls showing comparable very high activity, 15,000 and 12,000 units/gram respectively; both were cases of trichomonad vaginitis and enzyme levels fell to normal levels

following successful therapy. It is noteworthy that these 2 women also presented very high β-glucuronidase levels.

Two cases of "carcinoma *in situ*" of the cervix mentioned in the previous paper were also investigated in regard to α-mannosidase. The first, aged 40 years, gave readings of 5,600 and 5,500 units/gram at 1 month and 2 months after cervical biopsy had revealed an intra-epithelial carcinoma. The other patient, aged 51 years, showed an activity of 10,800 units/gram 6 months after an intra-epithelial lesion had been detected in the amputated cervix; she was still menstruating and subsequent biopsy failed to confirm the continued presence of a carcinoma *in situ*. This woman remains under close observation.

Women with Cancer of the Cervix after Treatment

In the β-glucuronidase series, enzyme levels were assessed at the follow-up clinic, but as this has not been done systematically in the case of α-mannosidase no useful information can be offered.

Correlation between Vaginal Fluid β-Glucuronidase and α-Mannosidase

Since the same women have been studied in respect of both enzymes, Tables III and IV have been prepared to show the results for both β-glucuronidase and α-mannosidase. In the pre-menopausal control group, some 70 per cent gave readings under 200 units/gram for β-glucuronidase *and* under 2,000 units/gram for α-mannosidase (called for convenience the "200–2,000" level). In very nearly 90 per cent of cases, the readings fell below the "400–4,000" level. Only 1 pre-menopausal woman gave a high (over 400 units/gram) reading for β-glucuronidase with a low (under 4,000 units/gram) reading for α-mannosidase. There were, however, 4 cases where the α-mannosidase level was high (over 4,000 units/gram) but the β-glucuronidase reading was low (under 400 units/gram). In 10 women (8 per cent) both readings were high, above the "400–4,000" level.

In the post-menopausal control group, some 23 per cent gave readings under the "200–2,000" level, and 50 per cent under the "400–4,000" level. As with the pre-menopausal women, it was rather unusual to find β-glucuronidase activity over 400 units/gram associated with α-mannosidase levels under 4,000 units/gram; but by contrast, 1 elderly woman in 4 gave high α-mannosidase and low β-glucuronidase levels.

Too much stress must not be laid on these figures as the numbers in the various sub-groups are small, but it would seem that there is very

TABLE III

Vaginal Fluid β-Glucuronidase and α-Mannosidase Activity in 121 Pre-menopausal Women without Gynaecological Cancer

β-Glucuronidase Units/gram		1–200 (98)	201–400 (12)	401– (11)
α-Mannosidase Units/gram				
Nil–2,000	(89)	84	5	0
2,001–4,000	(18)	12	5	1
4,001–	(14)	2	2	10

TABLE IV

Vaginal Fluid β-Glucuronidase and α-Mannosidase Activity in 56 Post-menopausal Women without Gynaecological Cancer

β-Glucuronidase Units/gram		1–200 (30)	201–400 (12)	401– (14)
α-Mannosidase Units/gram				
Nil–2,000	(13)	13	0	0
2,001–4,000	(17)	10	5	2
4,001–	(26)	7	7	12

TABLE V

Vaginal Fluid β-Glucuronidase and α-Mannosidase Activity in 20 Pre-menopausal Women with Cancer of the Cervix

β-Glucuronidase Units/gram		1–200 (4)	201–400 (2)	401– (14)
α-Mannosidase Units/gram				
Nil–2,000	(3)	1	1	1
2,001–4,000	(4)	2	0	2
4,001–	(13)	1	1	11

TABLE VI

Vaginal Fluid β-Glucuronidase and α-Mannosidase Activity in 22 Post-menopausal Women with Cancer of the Cervix

β-Glucuronidase Units/gram		1–200 (2)	201–400 (6)	401– (14)
α-Mannosidase Units/gram				
Nil–2,000	(2)	0	2	0
2,001–4,000	(5)	2	2	1
4,001–	(15)	0	2	13

little difference between the enzymes in pre-menopausal women, whereas in older women the trend towards higher levels is greater with α-mannosidase than with β-glucuronidase.

To complete the picture, Tables V and VI illustrate the situation in respect of both enzymes in pre-menopausal and post-menopausal women with cancer of the cervix. In the younger women, 11 out of 20 gave readings above the "400–4,000" level, compared with only 10 of the 121 controls. In the post-menopausal group, 13 out of 22 showed levels above "400–4,000", the comparable ratio for the controls being 12 out of 56.

SUMMARY

Results are presented to show that α-mannosidase occurs and behaves in the vaginal fluid, in health and in disease, in very much the same way as β-glucuronidase.

Appreciation is expressed to Mrs. Irene Rennie for technical assistance.

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PREGNANCY ASSOCIATED WITH HAEMORRHAGIC SMALLPOX

BY

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IN a country where smallpox is common, one would expect an association of smallpox with pregnancy to be a common occurrence. But a careful study of the available literature shows that not many such cases have been reported.

When smallpox affects a pregnant woman, it tends to become very malignant. The sudden onset of signs and symptoms and the short duration of the disease and the rapid termination make the diagnosis extremely difficult.

The interesting clinical features and unusual and unique pathological findings together with the difficulties we had in the diagnosis make it justifiable to publish such a case.

CASE REPORT

B., a Hindu aged 25 years and gravida-2 (hospital number 59220), was admitted to the Christian Medical College Hospital, Vellore, South India, on May 2nd, 1958, at 3 p.m., with the following complaints:

Amenorrhoea, 8 months.

Fever, 2 days.

Backache and labour pains since 7 a.m. that day.

Previous Obstetrical History. Her first pregnancy was a normal delivery at term 2 years ago. The child was alive and well.

Previous Medical and Surgical History. Nil relevant.

Condition on Admission. A well nourished woman of 25 years. Slightly anaemic, no oedema of the body. Heart and lungs, normal. Blood pressure 110/70. Urine, no albumin or sugar. Temperature, 99° F. Pulse, 90 per minute. Uterus, 32-weeks size. Foetal heart, 140 per minute.

Management. She was given penicillin injections, Codopyrine, and chloral and bromide mixture. She continued to have backache and had a restless night in spite of sedatives.

The following day it was noticed that her face was swollen and there was intense congestion of the face and the neck. Remembering that it was the season for smallpox we asked her whether she had been in contact with anybody suffering from smallpox or whether there were smallpox cases in her locality. She denied both.

Thinking that it might be due to idiosyncrasy to a drug, we suspended all the drugs. Temperature that day was 100° F.

On May 4th, 1958, at 7 a.m., purpuric haemorrhages were noted on her face, chest and extremities. To begin with these haemorrhages were very small and pin-point in size but later on became bigger, till some were as large as 1 to 2·5 cm. in diameter just before her death.

Samples of blood were taken for various tests. It was now noticed that the patient bled from every veni-puncture. There were sub-conjunctival haemorrhages also. Our tests included

estimation of fibrinogen. Blood transfusion was started and vitamin K was given. The haemorrhagic tendency increased. She had haematuria and bleeding from the gums. Thinking that it might be a rare case of hyperheparinaemia, protamine zinc sulphate and Toluidine Blue were given. She had had by now 2 pints of blood and 1 pint of gelatin. The condition progressed, haemorrhages under the skin and bleeding from the gums increased. There was no bleeding from the vagina. We noticed a few blebs about 3 to 4 in number on her extremities and these contained blood. She became restless and cyanosed, developed mental symptoms, became delirious and comatose and expired at 10.20 a.m., that is, 3 hours after the first appearance of petechial haemorrhages. The patient died undelivered.

Our diagnosis at that time was death from haemorrhage due to a blood disorder with a bleeding tendency.

The blood reports had not yet been received. A post-mortem was done and only then was the diagnosis of smallpox possible.

Investigations

4th May, 1958. Blood: White blood cells 67,400 per c.mm. Neutrophils, 50 per cent; eosinophils, 1 per cent; lymphocytes, 47 per cent; monocytes, 2 per cent.

Platelet count, 130,000 per c.mm. Prothrombin time, 1 minute 10 seconds (control 12·5 seconds—partial clot). Bleeding time, 3 minutes 20 seconds. Clotting time, 7 minutes 35 seconds.

Blood picture: moderate anisocytosis, moderate hypochromia and poikilocytosis, slight polychromasia, nucleated red cells, plus. Fibrinogen, normal.

Blood—Haemoglobin, 8·75 g. per cent on admission and 8·00 g. per cent at the first appearance of the petechial rash.

Post-Mortem Examination

The body was that of a pregnant female weighing 52·5 kilograms and 5 feet 1 inch in height. A well marked coppery red flushing of the face, the neck, anterior surface of the chest and the lateral surface of the upper arms was a striking feature. Haemorrhages in the skin varying in size from a pin point to about 1 cm. in diameter were scattered over the arms, the anterior surface of the chest and abdomen, thighs and dorsum of feet (Fig. 1). Most of these purpuric spots appeared to be in the deeper layers of the skin but close examination showed a few of the lesions to be slightly raised above the surface of the skin. Such lesions were found on the thighs and gluteal regions and strongly suggested early vesicle formation. On the left palm, at the roots of the little and ring fingers circular raised blebs containing blood, about 1·5 cm. in diameter, were seen. Similar blebs were also noticed at the tips of several toes, the largest of them measuring about 2·5 cm. in diameter. Some of these blebs were broken.

On the mucosa of the palate and inner surface of the lower lip, many irregular slate grey patches ranging in size from 0·2 cm. to 0·5 cm. in diameter, were present.

Marks of primary smallpox vaccination were present on the lateral surface of the right upper arm (Fig. 2).

Small haemorrhages were seen scattered on the visceral and parietal pleura, on the surface of the heart and on the endocardium, on the diaphragm, parietal peritoneum and over the entire mesentery. On the surface of the kidneys and on the mucosa of the bladder there were pin-point haemorrhagic spots. On the oesophageal mucosa there were slate coloured irregular patches of haemorrhage similar to those described in the palate. The serous and mucous coats of the stomach and the whole of the small intestine showed large patches of haemorrhage. The stomach and small intestine were filled with blood. The whole of the jejunum and the proximal one-third of the ileum showed a remarkable finding. The mucosa at this region was studded with innumerable clear vesicles 2 to 5 mm. in diameter (Fig. 3). These vesicles resembled very closely those seen on the skin in classical smallpox. These burst on pressure. The intervening mucosa showed patches of haemorrhage. The rest of the ileum showed innumerable irregular patches of haemorrhage. The caecum and colon showed no haemorrhage and did not show any vesicles.

The lungs were boggy, heavy and exuded

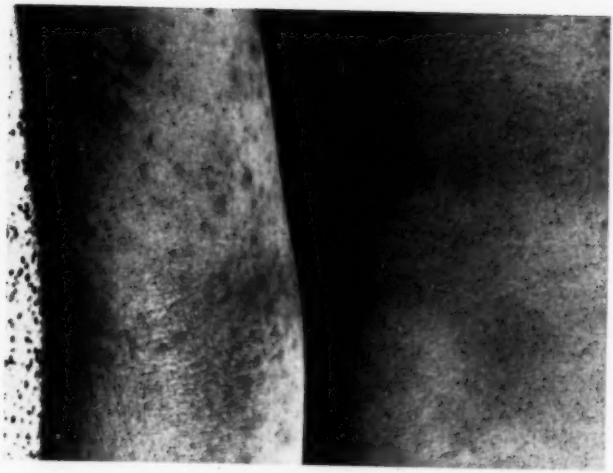

FIG. 1
Skin over the elbow region showing purpuric rashes.

FIG. 2
Prominent successful primary vaccination marks on the upper arm.

FIG. 3

Numerous vesicles on the mucosa of the small intestine.

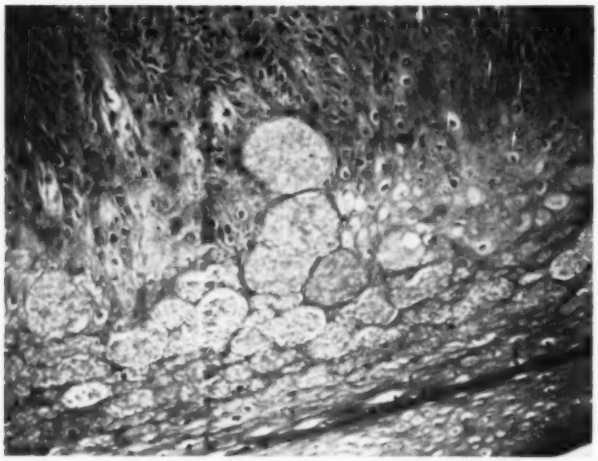

FIG. 4

Stratified squamous epithelium of palate showing typical reticular degeneration. H. & E. ×140.

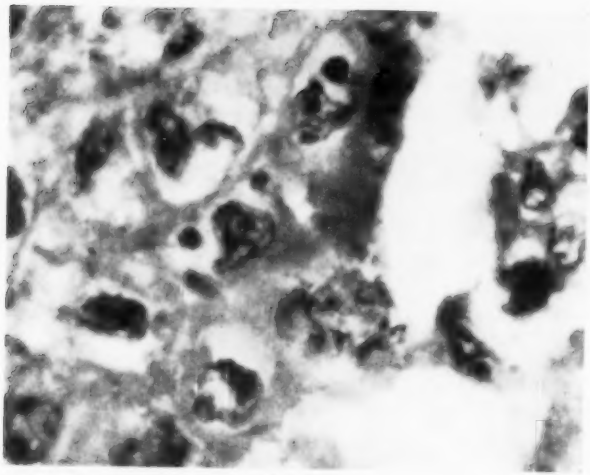

FIG. 5

Intracytoplasmic inclusion bodies (Guarnieri bodies). H. & E. ×1,400.

frothy fluid from cut surfaces. The liver was slightly enlarged, weighing 1,690 g. It was pale brown with slightly rounded edges and its cut surfaces showed several brownish white circular areas varying from 1 mm. to 7 mm. in diameter.

The spleen was very much enlarged, soft and congested and weighed 255 g.

The foetus weighed 1,800 g. It did not show any haemorrhage on the skin or other obvious lesions externally. Permission for autopsy examination of the foetus was not given.

Histological Findings

The stratified squamous epithelium of the skin, buccal mucosa and oesophagus showed the typical features of haemorrhagic smallpox. The epithelial cells were swollen, vacuolated and showed different degrees of degeneration; outlines of the swollen degenerated cells formed a reticulum containing in its meshes a haemorrhagic exudate (Fig. 4). In several places the supporting mesh work had ruptured forming larger spaces containing exudate. These spaces were breaking through the superficial layers of the epithelium to give an appearance of early vesicle formation. In the cytoplasm of these swollen epithelial cells were seen typical Guarnieri bodies determining the specificity of these lesions. These were round or oval, eosin staining structures varying widely in size from 1 to 8 microns in diameter (Fig. 5). Several cells contained two and three of these bodies. The epithelium also showed infiltration by a number of small round mononuclear cells.

The lungs showed well marked oedema. The alveolar walls were thickened and in several areas the alveoli contained lymphocytes and large macrophages.

The liver showed a moderately severe degree of fatty change, cloudy swelling of the liver cells and several small areas of necrosis. Many Guarnieri bodies were found in the parenchymatous cells. The portal tracts showed lymphocytic infiltration.

Sections from the jejunum and ileum showed fully formed vesicles in the mucosa. The epithelial cells were swollen and varying degrees of degeneration had set in. Most of the cells were completely necrosed.

Discussion

The autopsy findings, gross and microscopic, undoubtedly establish this case to be one of haemorrhagic smallpox. Two types of haemorrhagic smallpox have been recognized: (1) *Variola haemorrhagica pustulosa*, where the lesions mature to the vesicular or pustular stage and the haemorrhage occurs in and around these lesions; (2) a graver and a uniformly fatal form is the *purpura variolosa* where the disease manifests itself as a widespread purpuric rash and the patient dies before the typical rash of smallpox develops. The case presented here belongs to the latter group.

Some German authors believe that this type occurs almost exclusively in vaccinated people. Others do not agree with this. This patient had marks of successful primary vaccination. Another case of *purpura variolosa*, a man on whom we did a post-mortem examination, did not have any marks of vaccination. What is, however, very striking in this case is the presence of vesicles in the intestinal tract similar to those found on the skin in an ordinary case of smallpox. It is commonly postulated that in any severe form of smallpox the lesions may be manifested in a more intense degree in the gastrointestinal tract. However, authentic case reports of intestinal lesions in smallpox are few and we have been unable to find any report of a case with vesical formation. Councilman, Magarath and Brinckerhoff, as quoted by Rivers in 1948, from their wide experience with smallpox, state that the typical lesions are sharply limited to the stratified epithelium of the skin and of the mucous membranes of the soft palate, the pharynx and the oesophagus. Wolman (1951) reporting one case of *purpura variolosa*, mentions congestion and haemorrhages in the ileum and caecum but no vesicles. It is very interesting that when the lesions on the skin were just beginning to show vesicular degeneration, well formed vesicles had already formed in the gastrointestinal tract.

Microscopically, the so-called "reticulierende Degeneration" and "ballonierende Degeneration", seen in the stratified squamous epithelium of skin, buccal mucosa and oesophagus, were typical of any early lesion of smallpox. The pathognomonic cytoplasmic inclusion bodies

were seen not only in the epithelium of these areas, but also in the liver, spleen and intestines. The Guarnieri bodies ranged from 1 to 8 microns in diameter. First mentioned by Weighert in 1874, Guarnieri described these in detail in 1892, and believing them to be protozoan parasites, named them *Cytorcytes variolae*. The modern belief is that these are altered host-material containing numerous elementary bodies which are the causative virus of variola. Paschen (1906) described these structures and they are often named after him. These elementary bodies have a diameter of about 200 m. microns and are just visible under the microscope but in stained tissue sections their outlines are not discernible in the cytoplasmic inclusions.

Small foci of necrosis in liver, spleen and bone marrow are common accompaniments of haemorrhagic smallpox as in any other severely toxic disease.

The haemorrhagic tendency may be due to two factors. The numerous small necrotic areas in the bone marrow may suppress bone marrow activity and reduce platelet formation. The second and more important factor is the action of the powerful toxins on the capillary endothelium causing rupture of small capillaries.

Blood Picture

In the ordinary type of smallpox there is leukopenia with a relative mononucleosis but later a leucocytosis occurs. Anaemia usually occurs. In later stages depression of the bone marrow may result in alteration in the platelets, fibrinogen and prothrombin.

According to Musser (1951) in severe cases there may be an initial high leucocytosis and this may continue with an increase in the neutrophil polymorphs throughout the entire course of the disease.

In purpuric smallpox, on the other hand, the neutrophil polymorphs decrease although the total count remains high from an increase in the lymphocytes. Illingworth and Oliver (1944) mention a case where the leucocyte count was 18,000 per c.mm. on the second day and 38,000 per c.mm. on the fourth day. The differential count showed a leuko-erythroblastic blood picture without significant anaemia. Platelets are diminished.

Diagnosis

While the diagnosis of smallpox is not difficult in the majority of cases, the haemorrhagic type can be confused with such conditions as purpura and leukaemia and diagnosis may be extremely difficult. Bleeding from the mucous surfaces soon follows the cutaneous haemorrhages and in this case it occurred within 2 hours. Melaena and haemoptysis also may occur; they were absent here. Most workers stress the severe constitutional disturbances from the onset. Strangely enough in this case the constitutional disturbances were mild and the highest temperature was 100° F. In the fulminating type the patient may not survive long enough to develop the vesicular or pustular stage of the eruption. Death occurred in this case within 4 hours after the appearance of the purpuric rash. Large and irregular lesions are indicative of an extremely severe and uniformly fatal case and such cases are frequently undiagnosed. It has been suggested by some people that any case of fever with irregular purpuric lesions should be considered smallpox until proved otherwise.

Certain laboratory tests may be helpful in the diagnosis:

(1) A presumptive diagnosis could be made after microscopic examination of stained smears of a cutaneous vesicle or pustule for elementary bodies. We can expect to get the result in 1 hour. Stains should be freshly made.

(2) A final diagnosis could be made when the virus is isolated on the chorio-allantoic membrane. The growth on the chorio-allantois is found to be fairly dependable and sensitive and this test distinguishes variola from varicella virus. This test takes 3 days.

(3) The preliminary study of complement fixation tests in the diagnosis of these cases seems to yield reliable results. This test requires special hyper-immune serum.

(4) Paul's test—the contents of the pustule are applied to the scarified cornea of a rabbit. Opacities and intracellular inclusion bodies are noted in positive cases. This test requires 3 days.

Effect of Smallpox on the Foetus

Transplacental transmission occurs. Hence abortions, premature delivery, stillbirth and

neonatal death are common. Browne (1951) puts the stillbirth and neonatal death-rate as high as 80 per cent. The infant may be born with pock marks. It is said that the famous obstetrician Mauriceau was born with pock marks. If the mother had the disease for some time, the child may be born with healing pustules.

The children born of such mothers are said to be immune for some months and attempts at vaccination are not successful.

In this case, there were no pock marks on the foetus.

Vaccination

There is no contra-indication to vaccination during pregnancy, but it is not advisable to have it done in the puerperium for fear of introducing infection.

Prognosis

"In *purpura variolosa*, death is usually inevitable." Such a statement by Hunter (1956) indicates the grave nature of the disease. Similarly Sweitzer and Ikeda quote a mortality of 100 per cent in *purpura variolosa*. Gupta (1951) in Calcutta describes his experience with haemorrhagic smallpox in pregnancy. He treated 10 cases in all. The first 3 died before the rash appeared and diagnosis was completely missed. The rest of them had petechial haemorrhages and they all died. He also concludes that this malignant type of smallpox affected mostly pregnant women.

Herrlich (1959) in his report on an epidemic of smallpox in Bombay in 1958 mentions that the fatal course of *purpura variolosa* is unaffected by cortisone, acromycin or other antibiotics.

We could sum up best the present position as regards prognosis and treatment by quoting the Neapolitan paediatrician Michael Sarcone who wrote two hundred years ago: "The disease still defies all the efforts of the physician, and it is as malignant today as it was in the time of the Arabs who left us the first description of it."

Summary and Conclusions

(1) A case of haemorrhagic smallpox in pregnancy showing some unusual clinical features is reported.

(2) The post-mortem findings are reported and the pathological lesions are discussed.

(3) Laboratory tests may be helpful in the diagnosis of haemorrhagic smallpox.

(4) The pregnancy has an adverse effect on the disease. Haemorrhagic manifestations are common and are invariably fatal to mother and foetus.

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DIVERTICULUM OF THE FEMALE URETHRA

Report of Two Cases with Review of the Literature

BY

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THIS review of recent literature on diverticulum of the female urethra was suggested by two cases seen, one at the West Middlesex Hospital in 1951 and the other at Epsom District Hospital in 1959.

Case 1

Mrs. E.L.R., aet 37, attended complaining of deep dyspareunia for four and a half years dating from her first confinement and dysuria for 2 years from the birth of her second child. Otherwise she had no complaints and no symptoms referable to the urinary tract.

Pelvic Findings

As the patient strained the anterior vaginal wall prolapsed to the second degree but on palpation the "cystocele" proved to be a cystic swelling the size of a hen's egg beneath the epithelium of the lower third of the vaginal wall. It was not mobile, had no surrounding induration but was very tender. Such pressure on the swelling as the patient would allow produced no urethral discharge. The rest of the pelvis was normal. Urethral diverticulum was considered in the differential diagnosis.

A letter from the hospital *re* her second delivery stated: "When admitted in labour a 'cystocele' is reported as having been present since the first month of pregnancy. At this time attempted catheterization resulted in 'half-an-ounce of pus' being withdrawn."

On cystoscopy the bladder and ureteric orifices appeared normal. There was marked asymmetry of the trigone and the right ureteral opening was displaced posteriorly. This may have been due to displacement by the vaginal swelling. With pressure over the swelling cloudy fluid could be seen entering the bladder from the urethra.

The patient was admitted to hospital and, although there had been no history of recent acute infection in the diverticulum, was given penicillin (Distaquaine) 300,000 units 8-hourly for 48 hours before and after operation.

Operation was performed with the patient under a general anaesthetic in the lithotomy position. After catheterization the posterior wall of the urethra was palpated with a fine blunt probe which passed easily into the diverticulum through a hole 1½ cm. from the external meatus. The inside of the diverticulum was explored with the probe and appeared to be unilocular. During this procedure 3–4 ml. of opaque white odourless fluid escaped from the urethra. Simultaneously the diverticulum decreased in size. The probe was withdrawn and a metal sound passed into the urethra so that it should be easily identified.

The vaginal epithelium overlying the diverticulum was incised longitudinally for 2 inches and easily separated from it by gauze dissection. The diverticulum was mobilized laterally and inferiorly but was adherent to the urethra 4 cm. from the meatus.

The sac was incised and its inside inspected (Fig. 2). Two communications with the urethra were found 1½ and 3 cm. from the meatus. During further dissection the urethra was torn and these openings merged making a longitudinal split in the urethra 2 cm. long (Fig. 3).

The redundant diverticulum wall was excised and the urethra united over the sound by continuous No. 00 catgut. This layer was buried by

a further continuous suture in the fascia covering the urethra. Excess vaginal epithelium was removed and the urethra buttressed by mattress suture which included the vaginal muscle.

A soft rubber catheter was inserted and bedside drainage of urine allowed. Two days later the catheter became displaced and gentle attempts at reinsertion failed, but as the patient could pass urine normally the drainage was discontinued.

Two months later a wide bore rubber catheter could be passed easily. The patient had no complaints, no urinary symptoms and no dyspareunia. Six months later she was still without symptoms.

Histology showed the diverticulum to be lined partly by transitional epithelium which was extremely thin in places and partly by chronic inflammatory granulation tissue. The wall was formed by fibrosed muscle (Fig. 4).

The symptoms in this case began after the patient's first delivery and increased after the birth of her second child. It may be that the diverticulum was produced by trauma during the first confinement or it may have been of congenital origin and had been asymptomatic before delivery.

Case 2

Mrs. G.A.W., aet 49, complained for 4 months of the sensation of sitting on an egg. This could be relieved by pushing the tumour back into the vagina. She had had "recurrent cystitis" for 10–11 years with urge incontinence, and dyspareunia had increased recently. The patient had had a laparotomy performed for bilateral salpingitis 20 years before.

Pelvic Findings

The vagina was nulliparous and a cystic swelling 6 cm. in diameter was found in the middle third of the anterior vaginal wall. There was no prolapse and pus could be made to exude from the urethral meatus by pressure over the tumour.

Preliminary Investigations

Catheter specimen of urine: no growth. Urethral swab: no growth. Haemoglobin: 98 per cent. Gonococcal fixation test: negative. Intravenous pyelogram: "some irregularity of upper surface of the bladder looks like the result of extrinsic pressure."

Cystoscopy showed the bladder mucosa and trigone to be normal. Pus was stripped from the urethra on compressing the vaginal cyst.

Operation was performed with the patient under a general anaesthetic in the lithotomy position. The diverticulum was found arising from the middle third of the urethra and with difficulty it was manipulated to the introitus (Fig. 5). No communication with the urethra could be demonstrated by probing the posterior urethral wall. A catheter was placed in the urethra and a curved incision over the tumour was made to the right of the midline. The connection with the urethra was thought to be very small or tortuous as manipulation of the diverticulum produced very little pus from the urethra and no diminution in its size. As the sac was dissected free it was found to be loculated. One loculus was ruptured by accident, so the whole diverticulum was incised exposing its interior. No connexion could be demonstrated with the urethra but several cystic spaces were found close to the lumen. The wall of the diverticulum was very oedematous and densely attached to the urethra. The sac was excised and interrupted sutures placed in its base but the urethra was not opened. The urethra was buried by a further layer of interrupted catgut. The redundant epithelium over the mid-third of the vagina was excised and closed by mattress suture, away from the midline to avoid a suture line directly over the sutures in the urethral muscle. A Foley catheter was left in the bladder for 8 days. The patient passed urine normally after this and left hospital on the 13th day after operation. Two months later she had no complaints and her vaginal wall had healed, with no residual thickening.

The diverticulum was 2·5 cm. long and 1·6 cm. wide with a wall of rubbery consistency. The wall was formed of light textured collagen and the epithelium lining was partly transitional and partly squamous. Groups of foamy macrophages and foci of lymphocytes were in the outer part of the wall (Fig. 6).

It is interesting that this patient should be nulliparous as diverticula are far fewer in the

nulliparae, but in this case the congenital aetiology cannot be proved as it is possible that she had a urethral infection at the same time as her salpingitis which later led to stenosis of the orifices of one or more urethral glands with retention of their secretion.

Until 1938 diverticulum of the female urethra was seldom reported but then several series were published, mostly in the urological journals (Johnson, 1938; Parmenter, 1941; Higgins and Rambousek, 1945; Counseller, 1949; Wharton and Kearns, 1950). Each article stressed that the diagnosis had been made more frequently after the gynaecological and urological staff had been reminded that diverticulum of the female urethra could occur.

Although many series of cases have been published since 1950 (Gilbert and Rivera Cintrón, 1954; Lane, 1955; Nel, 1955; Pinkerton, 1956; Davis and TeLinde, 1958) the only recent article which could be found reporting cases treated in England was by Hennessy in 1958.

Aetiology

It was at first thought that there was a greater incidence of urethral diverticulum in coloured patients due to poor obstetric care and neglect of urethral infections (Herman and Greene, 1944; Menville and Mitchell, 1944) but later as more series were analyzed it seemed that the incidence did not vary with the percentage of white and coloured women in the community studied (Gilbert and Rivera Cintrón, 1954; Pinkerton, 1956).

There has been much debate about the aetiology of diverticula of the female urethra. Johnson (1938) classified them into congenital and acquired types.

Congenital

(*a*) Gaertner's duct.
(*b*) Cyst from faulty union of primal folds.
(*c*) Cell rests.
(*d*) Vaginal cyst.

Acquired

(*a*) Trauma during childbirth.
(*b*) Infection of urethral glands with sealing off and abscess formation later opening into the urethra.
(*c*) Instrumentation with deep fulguration of urethral lesions.
(*d*) Secondary to strictures of the urethra.
(*e*) Secondary to stone in the urethra.

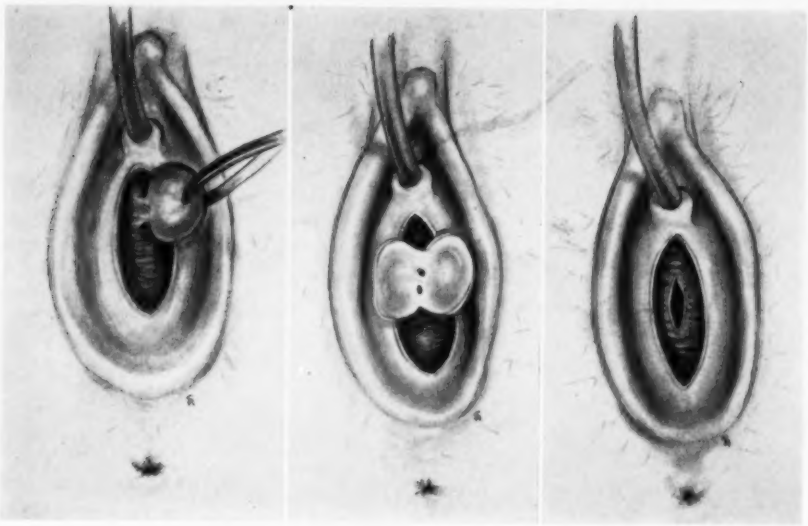
As most cases occur in parous women Higgins and Rambousek (1945) considered them to be acquired. Urethral diverticulum following a colporrhaphy, due to a fault in the suturing of the preurethral fascia in the region of the urethral sphincter, has been reported. Falls with the legs astride have been cited as an aetiological factor (Granberg and Svartholm, 1958; Hennessy, 1958).

Counseller (1949) believes that all diverticula originate from congenital defects which only give symptoms if infected or traumatized and that there are no glands opening into the urethra. Willmarth (1948) and Cook (1954) quote cases of ectopic ureters opening into diverticula. In Cook's case the ureter on one side proved to be duplicated and the one opening into the diverticulum was ligated. Diverticula are occasionally discovered in the newborn (Titcombe, personal communication, 1959).

The urethral glands are considered by many to be the female homologue of the prostate and have been demonstrated in foetuses by Folsom and O'Brien (1945) and Lintgen and Herbut (1946). Lintgen and Herbut studied 100 female urethras and were able to demonstrate the glands opening into the anterior urethra in all of these and the posterior urethra in 65; 76 showed histological inflammation. Huffman (1948) thinks that these glands will behave as all other glands and if their ducts become blocked will form cysts or abscesses. It is easy to believe that the majority of diverticula arise because of trauma to or infection of these glands.

Krieger and Poutasse (1954) made an excellent diagram to illustrate this theory.

Diverticula have been classified as true, where the diverticulum wall contains all layers of the urethra, and false (Kirby and Reynolds, 1949). Herman and Greene define a urethral diverticulum as a sac communicating with the urethra and lined by a continuation of the urethral mucosa. Other cavities similarly disposed but lacking an epithelial lining they call pseudodiverticula. The lining of epithelium may be



FIGS. 1, 2 AND 3
Stages in operation for diverticulum of the female urethra.

FIG. 4
Case 1. Diverticulum of the urethra. Lining partly transitional epithelium and partly granulation tissue. ×50.

FIG. 5

Case 2. Diverticulum of the urethra manipulated to the vulva.

FIG. 6

Case 2. Diverticulum of the urethra. Epithelium lining partly transitional and partly squamous. ×56.

squamous, transitional with occasional goblet cells or may be replaced by granulation tissue. Muscle fibres or glandular tissue may be present but in most pathological specimens the wall is fibrous with little or no muscle tissue. Chronic inflammatory changes are nearly always present. Diverticula may vary from a few millimetres to 2 inches in diameter and may extend to the base of the bladder or far laterally. They may be saddle-shaped across the urethra. The opening into the urethra may be large or minute, single or multiple and is usually in the floor of the middle third of the urethra. The vaginal epithelium over the diverticulum may be mobile or attached.

Symptoms

(1) *Pain*

This may be of four varieties (Counseller, 1949).

(*a*) Low abdominal or suprapubic similar to that of cystitis.

(*b*) Perineal extending to the rectum.

(*c*) Vaginal—a feeling of pressure or weight on walking or sitting.

(*d*) Urethral—pain darting upwards from the urethra.

(2) *Disorders of Micturition*

(*a*) *Dysuria.* Usually this occurs only when there is an associated urethritis or cystitis.

(*b*) *Sensation of Incomplete Emptying of the Bladder.* The patient may evacuate the diverticulum by digital pressure at the end of micturition.

(*c*) *Urethral Discharge.* Spontaneous leaking of pus or urine from the diverticulum may occur during intercourse or after micturition.

(*d*) *Haematuria.* This is rarely due to a stone in the diverticulum and is more often associated with acute cystitis or urethritis.

(*e*) *Urinary Obstruction.* This has been described in a child aet 23 months (Wharton and Kearns, 1950).

(3) *Dyspareunia*

This may be due to pressure on a large diverticulum or due to associated infection.

Diagnosis

Davis and TeLinde (1958) say: "The most important diagnostic instrument for the discovery of urethral diverticulum is a high degree of suspicion."

A diverticulum should be thought of when there is a story of recurrent attacks of cystitis or urethritis. Many patients are reported who have been treated for years and whose symptoms relapse when treatment is stopped.

The anterior vaginal wall and external urinary meatus should be inspected carefully. There may be visible swelling and pus may be seen exuding from the meatus. Palpation of the anterior vaginal wall from the base of the bladder to the external urinary meatus may confirm the swelling and induration may be felt. A firm catheter in the urethra sometimes assists in defining the mass. An attempt should be made to express pus or urine from the diverticulum into the urethra. The fluid so produced should not be confused with the small amount of physiological secretion which may sometimes be expressed from the normal urethra. The lesion may be so tender that pressure will not be tolerated. As the diverticulum may vary in size the patient should be examined on more than one occasion.

There may be pus and debris in a clean voided specimen of urine but none demonstrable in a catheter specimen from the bladder. This may be due to the urethral musculature squeezing the diverticulum at the time of voiding (Cook and Pool, 1949).

Urethroscopy may be performed with a dilating urethroscope. The orifice of the diverticulum is often difficult to visualize and may be obscured by granulation tissue or folds in the lining epithelium; occasionally it may be necessary to use a retrograde lens.

A straight X-ray of the base of the bladder and urethra may show calculi in the diverticulum. These can be mistaken for calculi in the bladder but are not found on cystoscopy (McMahon, 1946). Davis and TeLinde (1958) diagnosed 54 per cent of their cases by injection of radio-opaque fluid into the urethra and diverticulum. Positive pressure urography devised by Davis and Cian (1956), using the catheter designed by Taylor, enables small diverticula to be seen when no vaginal mass is

palpable. Diverticula have been visualized by coiling radio-opaque ureteric catheters in their lumina.

Treatment

The treatment of all urethral diverticula causing symptoms should be surgical but if the patient is unfit or refuses operation conservative methods may be tried. Non-surgical methods:

(*a*) Periodic dilatation of the urethra if there is coincident stricture.

(*b*) Urethral irrigations may help urethritis.

(*c*) Repeated digital evacuation of the diverticulum by the patient.

(*d*) Treatment of infection by chemotherapy and antibiotics.

Small non-infected diverticula may give no symptoms. If so they need not be treated surgically but should be reviewed from time to time (Higgins and Rambousek, 1945; Krieger and Poutasse, 1954).

Radical excision of the diverticulum can be performed as described in the two cases quoted by the following method:

(1) Insertion of a catheter or bladder sound.

(2) Exposure of the diverticulum through the anterior vaginal wall.

(3) Mobilization of the sac.

(4) Excision of the sac close to the urethra.

(5) Careful closure of the linear defect in the floor of the urethra.

(6) Closure of the vaginal fascia.

(7) Closure of the vaginal epithelium.

To avoid urethro-vaginal fistulae the vaginal epithelium should be trimmed so that its sutures are not superimposed on those in the urethra and vaginal fascia.

If there is sepsis the urethral opening of the diverticulum may be necrotic and it may be impossible to close it. Secondary repair should be performed when the sepsis has been treated. If the sac is very friable and adherent to the urethra it is wise to remove only part of it and to destroy the lining of the remaining part by carbolization or chemical cauterization (Wharton and Kearns, 1950). Ellik (1957) describes 7 cases in which the lining of the diverticulum was traumatized by "peanut" gauze sponge through a stab incision from the vagina and then packed with quarter-inch-wide strips of "Oxycel" gauze. This method is very suitable for sacs ramifying beneath the trigone and the entrance to the urethra need not be closed. Hyams and Hyams (1939) filled diverticula with ribbon gauze through an endoscope before mobilizing them and then inverted them with a number of purse-string sutures. Edwards and Beebe (1955) recommend incising the urethra to the external meatus and cutting away the part of the urethral wall containing the entrance to the diverticulum. They believe that the distal two-thirds of the urethra have little concern with the control of micturition but they do not disturb the proximal third of the urethra nor the base of the bladder. They reform the incised urethra over a catheter. For the rarer diverticula of the anterior surface of the urethra Gilbert and Rivera Cintrón (1954) suggest a suprapubic approach but do not recommend cystotomy to divert the urine.

Post-operative complications are thought by many to be few. Wharton and TeLinde (1956) report 3 urethrovaginal fistulae but they did not all cause symptoms. Krieger and Poutasse (1954) had 2 fistulae in 33 cases and did repeat operations for persistent diverticula.

Davis and TeLinde (1958) report 10 recurrent or persistent diverticula after operation and remark that 6 of these were noted to be multiple or compound type. They show urethrograms revealing only incomplete removal of a diverticulum.

Few series of cases have been followed by post-operative urethroscopy and Granberg and Svartholm (1958) give a more gloomy prognosis for the eventual results of operative treatment. They followed 17 of their patients (half of them for over 3 years) and of the 9 who were symptomless 2 showed recurrence of their diverticula and one a urethrovaginal fistula. X-ray studies of the total 17 showed recurrent diverticula in 7. One diverticulum persisted after three attempts at ablation.

Diverticulum of the urethra should no longer be considered a rarity but many cases require urethroscopic investigation before diagnosis is definite. Close co-operation between the gynaecological and urological departments is necessary to avoid duplication of investigations and there

is still a need for the staff of both departments to be made aware of this abnormality.

Summary

Two cases of diverticulum of the female urethra are presented with a short review of the current literature, including a discussion on the aetiology, symptomatology, surgical treatment and prognosis.

I wish to thank Miss I. M. Titcombe of the West Middlesex Hospital and Dr. W. D. Brown of Epsom District Hospital for permission to publish these two cases, Miss S. Robinson for her professional drawings and Mr. C. S. Ledwich for his photographic plates.

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THE PRESENT AGE OF THE MENARCHE IN SOUTHERN ENGLAND

BY

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It has been shown (Provis and Ellis, 1955; Tanner, 1955) that puberty is taking place in certain countries of Western Europe and in the U.S.A. at an earlier age now than a few decades ago. In the present report possible trends in the age of the menarche in Southern England during and since the second world war are examined.

In an earlier report (Wilson and Sutherland, 1950) the medical records of 202 girls who attended a boarding school in Sussex, and who left between 1936 and 1948, were studied; the age of the menarche had been entered on each record, and so the average age could be readily determined. The present average age of the menarche of girls at the same school has been obtained for comparative purposes by questioning 283 of the pupils in 1957. Each girl was asked her present age, and whether her monthly periods had started, the average age of the menarche being calculated by probit analysis. Similar information has been obtained from 1,029 pupils at county day schools in Sussex in 1957 for comparison with like data collected from 1,151 children attending county day schools in the nearby county of Dorset in 1949; Sussex children were not included in the earlier study (Wilson and Sutherland, 1950).

FINDINGS

The findings are summarized in the Table. In the Sussex boarding school the mean age of the menarche in 1957 was 13·30 years. For those who left the same school during the period 1936–48 the mean age was 13·11 years. The difference does not attain statistical significance, and so this comparison provides no evidence of any change in the mean age of the menarche since the second world war.

In the day schools in Sussex in 1957, the mean age of the menarche was 13·03 years. Although this figure is rather lower than the corresponding mean for the boarding school girls (the majority of whom are domiciled in counties other than

TABLE I
Average Age of the Menarche in Various Groups of School Children

Group of Children	Period	No. of Children	Mean Age of the Menarche (years)	Standard Error of the Mean Age (years)	Standard deviation of Age at Menarche (years)
Sussex boarding school ..	1936–48	202	13·11	0·09	1·21
	1957	283	13·30	0·18	1·95
Dorset day schools	1949	1,151	13·38	0·05	1·14
Sussex day schools	1957	1,029	13·03	0·06	1·25

Sussex), the difference is not statistically significant. There is thus no evidence that the age of the menarche in children resident in Sussex differs from that of a group of children whose homes are geographically more scattered.

The mean age of the menarche in Dorset day schools in 1949 was 13·38 years. In Sussex day schools in 1957 it was 13·03 years. This difference, of about 4 months, is statistically significant at the 1 per cent level, and it may therefore be concluded either that the menarche occurs rather earlier in Sussex than in Dorset, or that there has been a tendency since the second world war towards an earlier age of the menarche in Southern England, or that both these explanations have contributed to the difference.

Discussion

It is generally believed that the age of sexual maturation may be influenced by a variety of factors which include diet and environment as well as the genetic constitution of the racial group. Nevertheless, a number of recent studies have either failed to reveal differences when these might have been expected, or have revealed differences without any clear indication of the responsible cause. Thus no association is apparent between blood group and age of the menarche (Vuori, 1929; Grant *et al.*, 1956); there is no evidence that the age of the menarche in a low iodine area (North Oxfordshire) differs from that in other parts of Southern England (Hughes *et al.*, 1959); and there is a similar lack of association between the age of the menarche and factors of high emotional content such as ritual circumcision and initiation in West Africa (Wilson and Sutherland, 1955). On the other hand, data carefully collected by the same method as that used in England, in Nigeria, Central India, Ceylon (Wilson and Sutherland, 1953), West Pakistan and Northern India (unpublished) showed that in some of these areas the menarche occurred definitely earlier, and in some definitely later, than in England. Although it was clear that in these latitudes the age of the menarche was not determined primarily by climate, there was little positive evidence of the factors which were responsible. In some districts it is possible that a deficient intake of protein and calories may have delayed the menarche. However, deficiencies in trace elements such as iodine may be an unimportant influence in delaying the onset of the menarche if the diet is otherwise adequate. This lack of iodine is partly compensated by physiological enlargement of the thyroid gland (Hughes *et al.*, 1958). It is of interest in this connexion that in areas of low iodine intake thyroid enlargement is twice as prevalent in adolescent girls as in boys of the same age group. This is possibly connected with the additional stress brought about by the rhythmic metabolic changes imposed during the onset of menarche (Best and Taylor, 1958; Ten Teachers, 1959).

There is little reliable information on secular trends in age of the menarche in England and Wales. In a small series of 41 children living in a favourable social environment there was no apparent tendency for the menarche to occur at a different average age than in their mothers (Wilson and Sutherland, 1949). On the other hand, in Scotland Provis and Ellis (1955) found that the average age of the menarche in a representative sample of Edinburgh schoolgirls was 13·35 years, and a comparison with earlier (though less trustworthy) information supported the view that schoolchildren were maturing earlier now than at the beginning of the century. Tanner (1955) quotes the findings of retrospective enquiries in Norway, Sweden, Finland and in a women's college in the U.S.A., which show a remarkably similar trend, the menarche occurring earlier on average by one-third to one-half a year per decade over the period 1850 to 1950.

Against this background it is not easy to interpret the findings of the present enquiry. The one comparison in the Sussex boarding school, although it is the more precise, is based on small numbers; it shows no trend in age of the menarche, but it will be appreciated that there was probably no nutritional trend either. The other comparison, in the day schools, although geographically less precise and covering a shorter period of time, suggests that the menarche may now occur on average about 4 months earlier than it did a decade ago, a difference corresponding closely to the trend found by Tanner (1955). But it is also a plausible explanation that there has been no such trend, the difference being a matter of geography.

Acknowledgments

We have been helped by discussions with Dr. D. E. Hughes. We wish to thank the school medical officers in East Sussex and the doctors and teaching staff of the boarding school for their interest in the study and their readiness to make available the necessary medical records.

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THE PLACE OF PROGESTERONE IN THE TREATMENT OF ABORTION

BY

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As medical knowledge increases, so the causes of abortion are more readily determined, though there are still many cases where no cause can be found. It is in such cases that progesterone has been used empirically, with varying degrees of success.

In our present series we have used progesterone only on those patients who had a low urinary pregnanediol excretion.

The method of pregnanediol estimation used is essentially that of Sommerville, Marrian and Kellar (1948). Normal excretion levels are shown in Figure 1. Because this method is expensive in time, it was not possible to have as many estimations done as we would have liked. Could these have been done once a month throughout pregnancy we might have avoided some of the cases of premature labour, which occurred in 18 patients out of the 100 treated.

The choice of cases was also limited to the following groups:

(*a*) Patients who had had two or more previous abortions.

(*b*) Patients who had had one previous abortion and who were admitted to hospital with a threatened abortion.

(*c*) Elderly primigravidae, or previous cases of sub-fertility threatening to abort with their first pregnancy.

This estimation was done early in pregnancy, other causes of abortion having been excluded as far as possible.

When the pregnanediol level was low, progesterone treatment was given, but no special treatment was given when the level was normal or high.

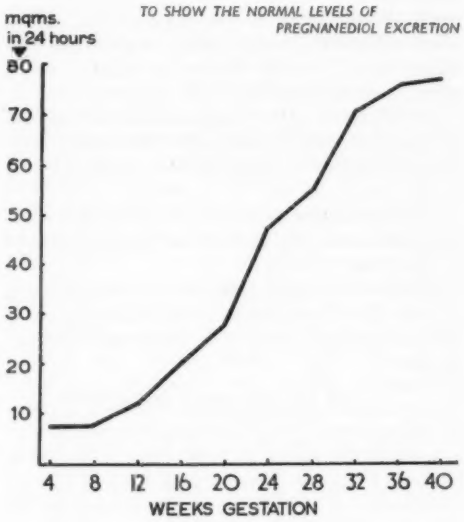

FIG. 1

When we first started these investigations no treatment was given to any case, and we have therefore a series of 40 cases of low pregnanediol excretion, untreated, to compare against 100 treated cases.

We are fully aware that 40 cases are too few for accurate comparison, but the difference in the two groups was too striking for us to feel

justified in trying to obtain a larger series of untreated cases.

There was also a series of 84 cases of normal or high pregnanediol level, which were left untreated.

Two methods of treatment were used, both allowing of a constant level of progesterone in the blood stream.

The first method was by implantation of 250 mg. progesterone through the fascia lata, and the second by a series of 8 intramuscular injections of "Primolut", which is a depot progesterone. In a few cases ethisterone was also given by mouth, but this method was less efficacious. The comparative results are shown in Figure 2.

Of the 40 cases of low pregnanediol which were untreated, 24 terminated in abortion, and there were 5 stillbirths or neonatal deaths, giving a total foetal loss of 72 per cent.

Of 100 cases of low pregnanediol treated with progesterone, there were only 3 abortions, with 10 stillbirths or neonatal deaths—a loss of only 13 per cent.

A comparative group of 84 cases of normal pregnanediol levels showed an abortion rate of 12 per cent.

Of the 9 neonatal deaths in the treated cases, 3 were due to prematurity and atelectasis, 1 to severe toxaemia, and 1 to accidental haemorrhage.

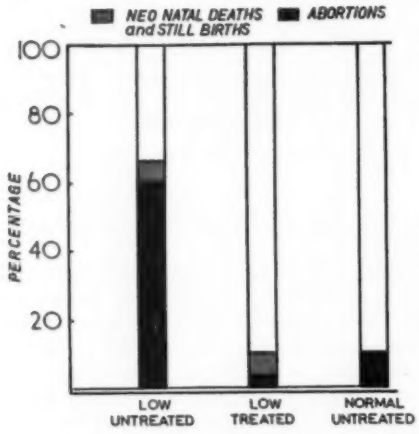

FIG. 2

There were 2 stillbirths in this group, one due to severe maternal influenza, and the second due to accidental haemorrhage after the patient had been run over by a lorry. This patient has since had a successful pregnancy following an implant of progesterone.

There were 10 cases of toxaemia in the treated group.

Perhaps the most outstanding case of the series was that of a patient who was admitted from London Airport, in the process of threatening to abort for the seventh time. She had had no children. She was treated with progesterone, and had a live baby. Following this she returned to her home abroad and had a further 2 miscarriages without treatment. Since then she had 2 more children after implants.

We offer this small series in the hope that others will be encouraged in the use of progesterone in cases of repeated abortion with low pregnanediol excretion. We feel that treatment should be continued as long as the level remains low, and that some of our losses through prematurity could have been avoided by giving more adequate treatment.

SUMMARY

Urinary pregnanediol estimations were done in 220 cases of threatened or repeated abortion. Forty cases with low pregnanediol were untreated and had a 60 per cent abortion rate and 12 per cent stillbirths or neonatal deaths. One hundred with low pregnanediol treated with progesterone had a 3 per cent abortion rate, with 10 per cent stillbirths or neonatal deaths. In 80 cases with normal or high pregnanediol which were untreated there was abortion in 9 per cent.

We wish to thank Dr. John Price, former Registrar at Hillingdon Hospital, who initiated the work, and also Mr. C. Allister and the staff of the Biochemical Department of the Hospital.

We are also grateful to Messrs. A. G. Schering who have taken an interest in the work, and supplied samples of Primolut.

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MATERNAL SYNDROME IN RH ISO-IMMUNIZATION

Report of a Case

BY

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MANY reviews and articles have been written on the subject of Rh iso-immunization concerning the complications which are liable to appear in the foetus and the newborn child. However, scant attention has been paid to the complications which might occur in the expectant mother, carrying a foetus severely affected by Rh antibodies.

In 1956, O'Driscoll first drew attention to the syndrome of fluid retention in the mother associated with severe iso-immunization to the Rh factor.

The clinical picture is very characteristic: massive pitting oedema in the dependent parts of the body and the lower abdomen, and occasionally blebs occurring in the striae gravidarum. There are no signs of oedema in the upper parts of the body. The oedema tends to develop rapidly over a few days and to disappear within hours of delivery. According to the author's account, if there is no cardiac or renal cause of the oedema and if the blood pressure and urinary findings are normal, the mother's condition is so typical that one can be certain that she is carrying a severely affected foetus.

Generally there is no albuminuria or hypertension, except in those cases where there is superimposed toxaemia of pregnancy. In O'Driscoll's cases the babies were severely affected; two of them were stillborn, and the third died 12 hours after delivery, in spite of an exchange transfusion. In all the cases the placenta was large and pale and the amniotic fluid was bile stained.

Goodlin (1957) described another group of cases with the same findings. According to him the signs are massive gain in weight, massive oedema especially in the dependent parts of the body (ankles, legs and lower abdomen), polyhydramnios, and sometimes generalized pruritus. There may be slight albuminuria and less frequently slight hypertension. Once this syndrome makes its appearance, he asserts that the foetal prognosis is virtually hopeless, the foetus dying *in utero* and the symptoms not subsiding until the pregnancy is terminated.

Potter (1947) states that there is a small group of women who show symptoms simulating toxaemia but in whom the condition appears to be specifically related to the existence of haemolytic disease. In these patients pregnancy usually progresses normally until the seventh or eighth month, and then a sudden rapid increase in weight is associated with visible oedema. A moderate amount of albumin is usually excreted in the urine. The systolic blood pressure almost never rises above 140. The foetus ordinarily dies soon after the onset of symptoms and is retained for varying lengths of time before it is delivered.

CASE REPORT

On 22nd May, 1957, a 27-year-old woman in the 8th month of her third pregnancy was urgently admitted to the ward with vaginal bleeding. The patient stated that a fairly severe haemorrhage without labour pains had commenced at home. Her obstetric history included two previous pregnancies. The first one was uneventful and she was delivered of a normal child by Caesarean section because of postmaturity. A number of days after the operation she

developed an acute abdomen with signs of cholecystitis, which subsided after conservative treatment.

In 1955, only one year after the Caesarean section, she was found to be 2-months pregnant and an abortion was performed on medical advice.

In the present pregnancy the last menstrual period was on the 22nd September, 1956, and the expected date of delivery was the 29th June, 1957. Her blood group was A-Rh neg. and her husband's B-Rh pos. The first child had been found to be A-Rh pos.

The course of the present pregnancy was quite normal until the 7th month, when oedema first appeared in the legs. The attending physician noted that at this time the uterine size was compatible with the duration of the pregnancy, and the foetal heart sounds were present. Urinary findings were normal. The B.P. was at the upper level of normal (130–140/90). The Wassermann and Kahn tests were negative.

A week before admission, her physician noted severe oedema of the lower limbs, and gave her Reserpine and a low-salt diet. Serological examinations of the blood gave a positive indirect Coombs' test and the incomplete Rh antibodies showed a titre of 1: 2048. On the day before hospitalization the oedema increased and involved the lower abdomen as well; urine examination was negative and the blood pressure 100/60. Foetal heartbeats were not heard.

On admission there was no vaginal bleeding. Severe oedema involved the ankles and legs and the lower abdomen, as well as the sacral area. The striae gravidarum were broad and tense. No other physical abnormalities were found, except the lack of foetal heartbeats. The patient remained in the ward for 4 days prior to delivery.

The following results were given by the laboratory examinations: haemoglobin 8·7 g. per cent; haematocrit 29·5 per cent; blood urea 13 mg. per cent; blood uric acid 3·5 mg. per cent; total protein 5·35 g. per cent; plasma sodium 147 mEq./l.; chlorine 105 mEq./l.; potassium 4·6 mEq./l. The titre of Rh antibodies was 1: 64 (complete) and 1: 256 (incomplete). (The difference in the titre of incomplete antibodies may be due either to different methods or to error.)

The patient was treated by bed-rest and acetazolamide (250 mg./day). The blood pressure remained stationary at 130–140/90, and large quantities of urine were passed.

On the 4th day of hospitalization, vaginal bleeding recurred with labour pains, and a partial placenta praevia was found on internal examination, the cervix being dilated to 3 cm. After amniotomy, labour progressed rapidly, and the dead child was delivered by craniotomy to avoid a prolonged 2nd stage after a previous Caesarean section. Two pints of blood were given before delivery.

The infant was macerated, with generalized oedema and the placenta was large and pale.

Twelve hours after delivery the oedema disappeared completely, the blood pressure was unchanged, and a blood count on the 3rd postpartum day showed 10·5 g. per cent haemoglobin.

Discussion

The main point is to differentiate this syndrome from toxaemia of pregnancy, not related to the blood incompatibility.

The clinical picture of severe oedema of the lower part of the body, with normal blood pressure and no urinary findings, is different from that encountered in cases of toxaemia with foetal death *in utero*.

The oedema of severe toxaemia generally involves, not only the lower half of the body, but the face and upper extremities as well. It develops slowly, as contrasted with its sudden appearance in this syndrome. In toxaemia the oedema subsides with the death of the foetus *in utero*, and not only after delivery.

The blood uric acid is usually high in toxaemia (Lancet and Fisher, 1956), whereas in our case it was within a normal range (3·5 and 3·8 mg. per cent). The high value of sodium and chloride in the serum is also unusual in toxaemia.

The aetiology of the syndrome is uncertain. O'Driscoll thinks that there is either an allergic reaction of the maternal body to the erythroblastic foetus or some unknown toxin produced by the affected foetus or placenta which gives rise to an increased permeability of the maternal capillaries.

The management of these cases has been disappointing, as the number has not been large enough to enable a way of treatment to be developed. Obstetricians should be on the alert for this maternal syndrome, and a method of treatment of the very first signs could thus be evolved.

Summary

The maternal syndrome in Rh iso-immunization is characterized by severe sudden oedema of the lower half of the body, without hypertension or albuminuria. Once these signs appear, the foetus is usually lost in spite of conservative treatment.

It can be differentiated from pre-eclampsia by the lack of the toxaemic triad and by laboratory examinations.

A case is reported which showed the characteristic clinical picture, with foetal death *in utero*.

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MYCOTIC VULVITIS

BY

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MYCOTIC vulvitis is generally acknowledged to be a rare condition, and when it occurs it is usually part of a more widespread vulvo-vaginitis. Very few cases of localized vulvar disease have been recorded in the past, for the condition does not readily persist unless fed from a vaginal focus. Most authors of standard text-books of dermatology and gynaecology make only passing reference to the subject, and Ormsby and Montgomery (1943), Whitehouse (1935), and MacKenna (1952) dismiss the monilial infections of the female external genitalia in 3, 10, and 11 lines respectively. Photographs of localized vulvar lesions are practically non-existent in the literature, and it is for this reason that the following three cases are recorded.

They are particularly interesting as they were all referred to a venereal diseases clinic, 2 of the cases closely simulating condylomata lata of syphilis, the third resembling ulcus vulvae acutum (Lipschutz's disease) (Lipschutz, 1923).

Case 1

This was a single woman, aged 21 years, who attended a Bristol gynaecological department on 9th September, 1957, with symptoms of acute vulvitis, frequency of micturition, and dysuria of 5-days duration. She strongly denied sexual intercourse but it was considered advisable to exclude specific infection, and she was therefore referred to the Maudlin Street venereal diseases clinic, which she attended on the same day. Clinical examination revealed two large and exquisitely tender erosions on the inner aspects of the labia minora. The ulcerative areas were identical in size and shape, and took the curious forms best described as holly-leaf in outline.

There was slight induration at the edges of the lesions but there was no evidence of granulomatous formation. Lymphangitic oedema of the labia majora was slight, and there was an entire absence of inguinal lymphadenitis. Vaginal examination was carried out with some difficulty owing to the acute tenderness of the lesions, but it was found that the vaginal mucosa was perfectly normal clinically, there was no vaginal discharge, and the cervix was quite healthy. In fact, the condition was distinctly localized and confined to the vulva (Fig. 1).

On questioning, the patient revealed that prior to the ulceration of the labia there had been "lumps" present, which had irritated intensely and which she had scratched violently in order to obtain relief. No local applications had been applied, and a chemical vulvitis could be ruled out.

Smears and cultures from the urethra and cervix were taken, but revealed no gonococci; and the blood Wassermann and Kahn reactions were negative. Dark ground examinations of the lesions were negative for trichomonads, spirochaetes and fuso-spirillary organisms. There was no evidence of enterobiasis and no lesions of the skin or other mucous membranes. Glycosuria was absent.

The past history revealed that in 1956 she had attended a Liverpool hospital for the treatment of trichomonal vaginitis. This had been successfully treated with Penotrane pessaries combined with Trichorad tablets orally; there had been no relapse. No other relevant features were noted in the past history.

The acuteness and severity of the vulvar ulceration invited an initial, tentative diagnosis of Lipschutz's disease, but this could not be supported microscopically as there was an entire absence of *B. crassus* from the lesions. Acute mycotic vulvitis was then considered to be a possibility and this was confirmed by the presence of woven mycelium and masses of long-branched filaments of Candida hyphae. Smears from the lesions were cultured on Sabouraud's agar and gave a pure growth of *C. albicans*. No yeast-like fungi could be isolated from the vagina or cervix.

Case 2

A married woman, aged 22 years, was referred to the Maudlin Street venereal diseases clinic, Bristol, on 5th June, 1958, from a gynaecological department. She was pregnant, and expecting her third child. The history was that of vulval swelling and irritation of 5-days duration, but she had suffered from vaginal pruritus for

the preceding 4 months. Her doctor had prescribed S.V.C. pessaries for the latter, but no relief had been obtained. The past history was otherwise uneventful.

On examination, vulval lesions were present which were highly suggestive of syphilitic condylomata lata. There were exuberant granulomatous nodules on both labia majora, decidedly indurated, and oozing serum copiously from the surfaces. The smaller lesions were circular in outline, slightly umbilicated, some having raised "button-rim" edges and thin areolation; the larger lesions had become matted and confluent, forming an indurated, partly-sloughing mass of inverted horse-shoe shape, which appeared to surmount the upper half of the external genitalia (Fig. 2). The labia minora were largely spared from this condylomatous process, but were intensely injected. There was, however, an absence of tenderness on palpation in all areas. Inguinal adenitis was not present, there was no intertrigo of groins or peri-anal skin, and no other external lesions of the body. Vaginal examination revealed a very severe thrush infection involving the whole of the inner two-thirds of the vaginal mucosa together with the cervix. Exclusion tests for venereal infection were negative and there was no evidence of trichomoniasis. Smears from the vulval nodules revealed no fungal elements, but cultures from the same lesions produced a pure growth of *C. albicans*. There was no glycosuria in this case.

Case 3

A single Jamaican woman, aged 28 years, attended the casualty department of the Gloucester Royal Hospital on 7th October, 1958, complaining of severe dysuria of 4-days duration.

On examination, the casualty officer found that she had numerous greyish, condylomatous lesions of the vulva, and, having elicited that there had been multiple recent sexual exposures, came to the reasonable conclusion that the condition might well be syphilitic.

The patient was therefore transferred to the venereal diseases clinic, which she attended the following day. There it was noted that she was febrile—100·2° F., and that she had the utmost difficulty in walking owing to severe pelvic discomfort. Clinical examination was most difficult, as digital attempts to display the vulvar lesions produced intense pain and had to be abandoned. The patient was therefore admitted into hospital forthwith for fuller inspection under sedation. It was then discovered that she had a widespread condylomatous, pseudo-syphilitic involvement of almost the entire vulvar epithelium and vaginal introitus. There was a prominent, brawny bilateral oedema of the labia majora, with multiple chancrous erosions and sloughing papules along the inner borders and interlabial grooves. The labia minora, vaginal vestibule, clitoris and fossa navicularis were extensively infiltrated by irregular ulcers covered with an indurated greyish-white base and surrounded, in the majority, by a bright red inflammatory areola. The size of the lesions varied from 5 to 15 mm. across, the smaller ones being definitely round in outline, flat-topped and with slightly shelving edges (Fig. 3). Coalescence of some had given rise to sessile vegetative plaques which exuded a muco-purulent discharge. Speculum examination of the vagina was essentially negative, and the cervix was clinically normal. Inguinal adenitis was strangely absent, and there were no lesions of skin or mucous membranes elsewhere.

Exclusion tests for venereal diseases were carried out; there was no evidence of gonorrhoea, syphilis, or chancroid.

Smears from the lesions revealed tangled mycelial threads with yeast-like budding, and *C. albicans* was cultivated on Sabouraud's medium.

As in the two previous cases, there was an absence of glycosuria.

Discussion

Wilkinson reported the presence of yeast-like organisms in vaginal discharge in 1840, which was the year after Langenbeck had discovered the fungus in cases of oral thrush. Prior to 1931, only isolated reports on mycotic vulvo-vaginitis had appeared in the literature, for the disease was not regarded as common. It is difficult to assess the true incidence of the genital mycoses, but it is generally thought that about 10 per cent of women harbour yeast fungi, and the majority of these females are asymptomatic carriers. Dawkins *et al.* (1953) found *C. albicans* in 8 per cent of 500 women attending family planning clinics, of whom none had vaginal symptoms. Campbell and Parrott (1950), in a study of 836 consecutive gynaecological patients, found that 15·9 per cent harboured *C. albicans*, and of these only one-third had symptoms or signs that might be attributed to yeast vulvo-vaginitis. Weinstein and Wickerham (1938) found an incidence of 7·3 per cent in asymptomatic, non-pregnant women. On the other hand, Castellani (1929) stated that in normal women of clean personal habits fungi are not found, or are extremely rare. The incidence of asymptomatic infection in pregnant women is generally agreed to be three to four times as great as in non-pregnant females. Carter and Jones (1937) claimed that 43 per cent of their antenatal cases harboured yeast fungi, while other workers have reported even higher incidences.

The reported frequency of mycotic disease of the female genital tract varies in proportion to the recognition of the symptoms and to the facilities used for diagnosis. The presence of saprophytic fungi, which cannot be differentiated from *C. albicans* without the use of

cultural methods, may sometimes be present and add to the difficulties of diagnosis. There are three common genera of yeast-like fungi which may be found in the vaginal tract, the separation of these being based on the morphological characteristics when grown on Sabouraud's agar. Of these three genera, saccharomyces and cryptococcus are considered to be non-pathogenic, while of the third genus Candida, which consists of five species, only *C. albicans* is definitely pathogenic in the vagina. The latter organism, therefore, is by far the most common cause of yeast vulvo-vaginitis (Ramsbottom, 1931).

Monilial infection of the genital tract may or may not lead to the development of thrush-like patches. In some cases there is merely mucosal reddening and an entire absence of the curding or felting which is generally associated with mycelial mould-like growths. In other cases there may be an intense vulvo-vaginal hyperaemia, with the occasional development of granular mucosae. The itching, burning and smarting produced may involve the adjacent skin of the groin and perineum, leading to severe degrees of intertrigo. Rarely secondary infection supervenes, with furunculosis and superficial ulceration. Local oedema may be present, but satellite adenitis is not a feature. Cystitis has been recorded but other complications are rare, and there is no evidence that yeast fungi become pathogenic in the higher reaches of the urogenital tract. It is most unusual for the genital condition to progress to granulomatous or condylomatous formation, such as described in Case 2 and Case 3, and the only comparable case which I can find in the literature was described by Moench in 1929. This was a woman aged 25 years who had diffuse and painful growths on the vulva and within the introitus, producing a distressing, lancinating type of pain. The condition was thought to be diphtheritic, as the condylomatous lesions were bathed in tenacious mucus and within the vagina were confluent, involving the whole canal in moist, papillomatous outgrowths. The cervix, too, was involved. Culture on Sabouraud's medium clinched the diagnosis of thrush, and produced a pure growth of *C. albicans*. Moench's case was interesting in that it was resistant to all methods of treatment until 1/1000 gentian violet was applied topically and in douches.

The differential diagnosis of mycotic disease of the female genital tract is particularly varied, and embraces trichomoniasis, non-specific and specific bacterial infections, chemical vulvo-vaginitis, venereal diseases (syphilis, gonorrhoea, chancroid, lymphogranuloma venereum, granuloma venereum), herpes progenitalis, Lipschutz's disease, malignant conditions, aphthous vulvo-vaginitis, ulceration from trauma, enterobiasis, genital scabies and pediculosis, atrophic vulvitis, leukoplakia, genital tuberculosis and diphtheria, Hodgkin's disease, eczema and neurodermatitis, and, in fact, any lesion which produces pruritus vulvae or ani. Diabetes mellitus and renal glycosuria of pregnancy are definite predisposing factors, and a high vaginal acidity favours the growth of Candida. The condition is commoner in parous women, but not unknown in children, virginal adults and senile women. The role played by individual sensitivity is not understood, nor is the variation in pathogenicity of fungi of the same species. Delivery usually leads to complete relief in pregnant women, while the onset of menstruation generally has an alleviating effect (Plass *et al.*, 1931).

Balano-posthitis has frequently been observed in the husbands of women suffering from vaginitis due to *C. albicans* (Harkness, 1950; Waisman, 1954). This may take the form of an isolated lesion of the glans and prepuce, which may be covered with a greyish-white felting of mycelium, or there may be an associated urethritis due to the fungi. The husband of Case 2 had an erosive balanitis of several months duration, associated with itching, but there was no concomitant urethritis. *C. albicans* was ultimately isolated by cultures from the penile lesions. This was undoubtedly a case of conjugal infection, and the condition rapidly cleared with topical applications of 1 per cent aqueous solution of gentian violet.

In all the 3 cases of mycotic vulvitis described, treatment consisted solely of applications of gentian violet in 1 per cent aqueous solution. There was complete restoration to normal in 15, 21, and 25 days respectively, and no relapse has so far occurred in any of the three women.

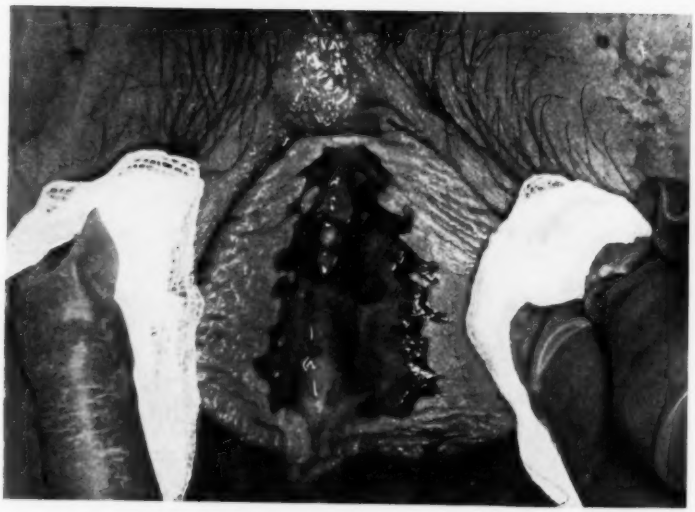

FIG. 1

Case 1. Single woman, aged 21 years. Acute vulvitis due to *C. albicans*, showing symmetrical ulcerative lesions of the labia minora. The condition was confined to the vulva.

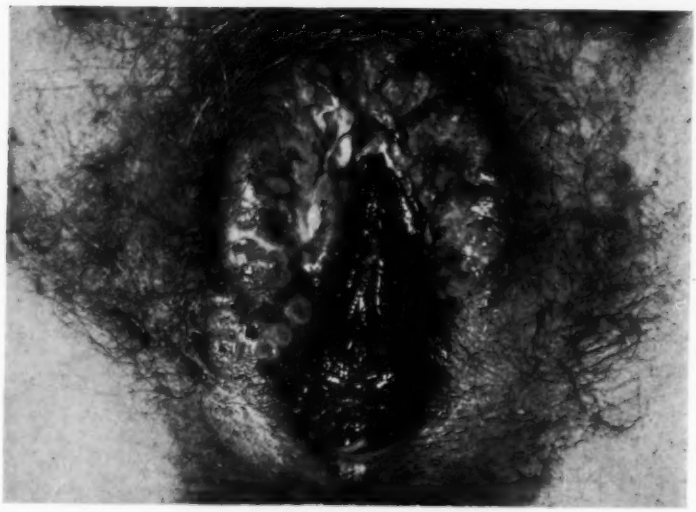

FIG. 2

Case 2. Married woman, aged 22 years. Pseudo-syphilitic granulomata of the labia majora due to *C. albicans*. Typical thrush lesions were also present in the vagina. Conjugal monilial balanitis was present in the husband.

FIG. 3

Case 3. Single Jamaican woman, aged 28 years. Multiple chancrous erosions and pseudo-syphilitic sloughing papules of the vulva due to *C. albicans*. There was no vaginal involvement.

Summary

Three cases of mycotic vulvitis due to *C. albicans* are described. In 2 of these the condition was entirely confined to the vulva; in the third there was an associated thrush vaginitis.

All 3 cases were referred to a venereal diseases clinic, there being close mimicry of syphilitic condylomata in 2 cases, the other having a condition simulating Lipschutz's disease.

Thrush infections of the external genitalia may resemble the secondary stage of syphilis so closely that only by microscopical, serological, and careful clinical examination over the full period of incubation (3 months) may the latter be finally excluded.

In diagnosing genital thrush, reliance must not be placed on slide diagnosis only; in Case 2 the organism was only discovered by cultural methods. It must also be remembered that staining solutions may be contaminated by fungi. Harkness quotes his own and Janet's experience that fungi may develop in aqueous solutions of methylene blue and neutral red. The former author recommends a small crystal of thymol in the stock bottles to inhibit the development of fungi.

In the 3 cases described, conjugal infection occurred in the husband of one, producing a chronic balanitis.

The treatment of election is considered to be the topical application of 1 per cent aqueous solution of gentian violet. With this treatment alone there was complete restoration to normal in an average of 20 days.

The rarity of illustrated cases in the literature is noted.

I should like to express my gratitude to Dr. A. E. Tinkler, Consultant in Venereal Diseases, Bristol Clinical Area, for his helpful advice in recording these cases, also to the staff of the University of Bristol Medical Photographic Unit, for supplying the excellent photographs.

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A CASE OF AMOEBIC VAGINITIS

BY

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AMOEBIC infestation of the vagina is a rare condition and is of sufficient interest to be recorded. The symptoms are similar to those accompanying trichomonal vaginitis, but on examination there are found ulcerative lesions on the vaginal walls and frequently on the cervix. Weinstein and Weed (1948) in a report on vaginitis due to *Entamoeba histolytica*, state that though a search of the literature from 1916 to 1946 revealed only 10 cases of vaginitis due to this organism, their 4 cases were discovered in a period of 9 months. The treatment they used consisted of vioform powder in the vagina and emetine and streptomycin systemically. Other workers have reported success with aureomycin and bacitracin (Crossen, 1953).

CASE REPORT

The patient, Z.H., aged 25 years, had been married for 9 years, having had one abortion and 5 full-time normal deliveries; all the babies were alive and well, the last being 9 months old. She was still breast-feeding this baby and had not yet begun to menstruate after the delivery.

She gave a history of amoebic dysentery for 7 years previously, with acute exacerbations which had been repeatedly treated. There was no history of other serious illness, blood transfusion or operation.

The history of her present complaint was:

(1) Pain in the lower abdomen with a sense of bearing down.
(2) Soreness in the vagina and dyspareunia.
(3) A copious badly smelling vaginal discharge.

All these symptoms had been present for a period of 7 months. She had not had any exacerbation of amoebic dysentery for the previous 12 months.

ON EXAMINATION

Her general condition was satisfactory, she was not anaemic or jaundiced. Her temperature was 99° F, the blood pressure 115/75 mm. Hg, and the cardiovascular and respiratory systems were normal. The abdomen was distended with a slightly tender caecum, but the liver and spleen were not palpable.

On vaginal examination there was found an excessive and offensive sanguino-purulent vaginal discharge. The vaginal walls were rough and tender and studded with small irregular ulcerative lesions with indurated bases. The cervix was healthy and soft. The uterus was anteverted and mobile, being the size of a 10-weeks pregnancy and soft in consistency. Although the patient was lactating, she appeared to be about 10-weeks pregnant.

The following investigations were carried out:

(1) A vaginal swab was taken which showed the presence of a heavy infection of active *E. histolytica*.

(2) The pH of the vagina was 8·5.

(3) A blood count showed: R.B.C. 3,900,000 per c.mm. Haemoglobin 78 per cent. White cells 8,300 per c.mm. The differential count was: polymorphonuclear leucocytes 52 per cent, lymphocytes 38 per cent, eosinophiles 6 per cent, and monocytes 4 per cent.

(4) Sigmoidoscopy was performed by Professor H. Morgan, who reported: "View impaired by soft flecks of faeces adherent to the walls. Sigmoidoscope passed to 8 inches. The lining of the rectum appears surprisingly normal. There is some pitting of the rectal valves which is found in amoebic dysentery and other conditions. No other evidence of amoebiasis was found. Small internal haemorrhoid at 5 o'clock was seen. Scrape from rectal wall showed no *E. histolytica* vegetative forms."

(5) Repeated examination of the stools for *E. histolytica* gave negative results.

Treatment

The patient was admitted to hospital.

Emetine gr. ½ was given on the first day, increasing to 1 gr. daily for 7 days, making a total dosage of 7½ gr. Streptomycin 1 g. daily was given for 5 days with Camoform (bialamicol hydrochloride) 250 mg. tabs t.d.s. Viozol vaginal pessaries 2 daily were inserted for 10 days.

Four days after the beginning of the treatment active amoebae disappeared, the vagina became much less tender on examination and the vaginal discharge lessened.

Six days later the patient was discharged from hospital, the vaginal wall had almost healed and the discharge was whitish and less offensive, although it was still seen to contain amoebic cysts microscopically.

Progress

Fifteen days later the patient reported for a check up examination. She was free from symptoms and the vaginal walls appeared normal. Vaginal swabs showed no active amoebae or cysts. She was then 14-weeks pregnant.

She returned 14 weeks later suffering from hydrorrhoea, and this was followed by the premature delivery of a 28-weeks living child. Vaginal swabs taken on this occasion showed no evidence of active or vegetative forms of amoebae.

Summary

A case of amoebic vaginitis, a very rare condition, is described. Anti-amoebic treatment appeared to produce a complete cure of the condition.

Acknowledgments

My thanks are due to Dr. Ahmed Ali Zaki, Director Medical Services, Sudan, for permission to publish this case, and to Professor G. Daly, Professor of Obstetrics and Gynaecology, and Professor H. Morgan, Professor of Medicine, Khartoum University, for their encouragement. I would like also to thank Ed Daw Ali Mohamed, the local Laboratory Assistant, who discovered the amoebae whilst examining the swab.

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ROYAL COLLEGE OF OBSTETRICIANS AND GYNAECOLOGISTS

At the meeting of Council held in the College House on Saturday, 26th March, 1960, with the President in the Chair, Mr. T. N. MacGregor was appointed Sims-Black Professor to visit Australia and New Zealand in 1961.

CONFERENCE OF THE INTERNATIONAL SOCIETY OF GEOGRAPHICAL PATHOLOGY ON "ECLAMPSIA AND PRE-ECLAMPSIA IN PREGNANCY"

It is regretted that there was an error in the President's Letter announcing this Conference. The date is not in September but *28th–30th June, 1960.*

FIRST INTERNATIONAL CONFERENCE ON CONGENITAL MALFORMATIONS

London, 18th to 22nd July, 1960

Honorary Presidents: Basil O'Connor (U.S.A.) and Sir Geoffrey Marshall (England)

General Chairman: Professor J. D. Boyd (England)

This Conference will be held at Church House, Dean's Yard, Westminster, London, S.W.1.

Eight sessions will be held during the Conference, the programme of these being arranged by the Scientific Programme Committee. Invitations to present scientific papers have been issued through the International Medical Congress, Ltd., by the Scientific Programme Committee. Time will be allowed for general discussion of these papers. The official languages of the Conference will be English, French and German. There will be simultaneous interpretation of each address into the three languages.

Correspondence and enquiries should be addressed to the Secretariat, 67 New Bond Street (Dering Yard), London, W.1. Telegrams: Conmal Wesdo London. Cables: Conmal London.

BOOK REVIEWS

"Physiotherapy in Obstetrics and Gynaecology." Revised by MARIA EBNER. 2nd edition. Pp. xii+244, with 97 figures. Livingstone, Edinburgh and London, 1959. Price 20*s*.

THE new edition of the late Helen Heardman's book, revised by Maria Ebner, contains as additional material chapters on applied anatomy and physiology and a statistical review of the results of an "education for childbirth programme". This last purports to show that physical as well as emotional advantages accrue from such a programme; perhaps partly because the physiotherapist is expected to attend the patient during as well as before labour. This is a most useful book for study by all who attend pregnant women, particularly by physiotherapists and midwives. Obstetricians might hope to see in the next edition an enlargement of the short but tantalizing chapter on "The Induction of Labour by Physiotherapy".

"Endocrine Aspects of Breast Cancer." Edited by A. R. CURRIE. Pp. xvi+340, with illustrations. Livingstone, Edinburgh and London, 1958. Price 37*s*. 6*d*.

THIS is a record of the proceedings of a conference held in Glasgow University in July, 1957. Four aspects of the subject were discussed—clinical, pathology, hormone studies and experimental pathology. Each section concludes with an admirable summary. The editor and his colleagues, and the publishers, are to be complimented on a volume well and quickly produced.

"Lehrbuch der Gynäkologie." By ROBERT SCHRÖDER. 5th edition. Pp. xviii+506, with 464 illustrations. VEB Georg Thieme, Leipzig, 1959. Price D.M.48.

ALTHOUGH this is the fifth edition of a standard textbook, it is in fact a new work. The first edition was published in 1922 and the fourth edition in 1945. This latest edition, and the first to appear since the war ended, has been prepared by a different publisher. As a consequence the text has been extensively revised, the illustrations changed and augmented and the lay-out altered.

The textbook is designed for students and practitioners, rather than specialists, and discussion of technical details and disputed questions is therefore avoided. Operative techniques are not described. The contents and plan of the book are conventional. Introductory chapters concerning the normal anatomy and physiology are followed by descriptions of the disorders of the menstrual cycle, anomalous positions of the pelvic organs, vaginal discharge, inflammatory disorders, endometriosis, sterility, injuries of the genital tract and congenital malformations. Tumours of the female genital tract are described in chapters devoted to cysts, ovarian tumours, myomata and fibromata, sarcomata, adenomata and polyps and finally carcinomata. The two concluding chapters deal with disorders of the urinary tract and the place of the gynaecologist in the prophylaxis of disease in women. Professor Schröder's abiding interest in gynaecological pathology is apparent, and his descriptions of morbid anatomy and histology are particularly valuable. The photomicrographs are well chosen, only occasionally do they fail because too low a magnification has been used to show the detail required. It is to be regretted however that most of the gross pathological anatomy is represented by drawings rather than photographs of actual specimens. References to the literature are confined to those that the author has considered of particular importance.

Most of the opinions expressed and the treatments advised are acceptable. However, for the British reader, a strange note is struck by the repeated references, particularly in the treatment of deranged hormonal function and inflammatory conditions, to specific dietary regimes, hydrotherapy and special exercises. The use of both radium and radiotherapy in benign conditions is often advocated as the treatment of choice. Ventrofixation is discussed as a method of treatment of uterine prolapse. Sub-total hysterectomy is recommended for the removal of fibroids in women under the age of 45 in whom the cervix is healthy and where myomectomy is technically impossible. As might be expected from the pen of the man who has made fundamental contributions to the subject, the chapter on "functional" uterine bleeding is very clearly written. Although one is surprised to find no mention of the place of hysterectomy in the treatment of such cases which are refractory to curettage and hormone therapy. The consideration of endometriosis is disappointing and the problems of its treatment are neglected. The description of congenital abnormalities of the female generative organs is masterly and the defects of embryogenesis which produce them are lucidly explained and well illustrated by diagrams.

German undergraduates and practitioners must be grateful that Professor Schröder, who died within a few days of its publication, was able to complete the preparation of the 5th edition of his textbook, which is worthy of the man and will surely remain as a monument to him.

Peter J. Huntingford

"Proceedings of the 32nd Conference of the German Society for Gynaecology at Frankfurt am Main, 16th–20th September, 1958. (Verhandlungen der Deutschen Gesellschaft für Gynäkologie. 32. Versammlung abgehalten zu Frankfurt a.M. vom 16. bis 20. September, 1958.)" Edited by H. KIRCHHOFF and A. W. SCHWENZER. *Archiv für*

Gynäkologie. 1959, **193**. Pp. x+525. Published by J. F. Bergmann, Munich. Price D.M.35.

THIS volume contains the texts of 92 of the 117 papers and the points of view expressed in discussion, which were presented to the Society during the three and a half working days of the Conference. Most of the contributions were from West Germany, but German-speaking representatives from Austria, East Germany, Greece, Holland, Hungary, Jugoslavia, Poland, South America, Spain, Sweden, Switzerland, Turkey and the United States also read papers. The President of the Conference was Professor H. Naujoks, whose untimely death in September, 1959, is a source of great regret.

The first of the main themes discussed was the female climacteric. The subject was introduced by reviews, which presented the points of view of a physician, a gynaecologist and a psychiatrist. The papers which followed dealt with different aspects of the climacteric and the disturbances accompanying it. The contributions fall roughly into two groups: those dealing with the hormonal changes and those devoted to a study of the alterations in the autonomic nervous system. Valuable contributions were made, but no new principles were stated.

The second symposium was concerned with the auxiliary methods of treatment of cancer, and was opened by Professor Runge with a review of the effects of the sex hormones in cancer of the female genital organs. He has obtained encouraging results by using oestrogens before radical surgery or radiotherapy in the treatment of carcinoma of the cervix. H. W. Vasterling then reviewed the chemotherapeutic agents that can be used against cancer cells. Their place has not yet been established in the primary treatment of genital cancer, but as adjuvants to treatment in cases of recurrence they have been found useful. Further reviews considered general supportive measures, the palliative surgery of genital carcinoma and the treatment of urinary fistulae caused by malignant disease or the treatment of it. There followed a series of papers on the results obtained by using various hormones and chemotherapeutic agents in the treatment of female genital cancer.

The reviews and papers, which were read concerning the physiology and pathology of uterine contractions, are summarized (the complete texts of these papers are to appear in the 2nd volume of *Bibliotheca Gynaecologica*, published by Karger, Basel). The reviews concerned tocography and tocodynamometry and the method of recording the progress of labour by "Partogramms" as devised by Professor Schwalm. Twenty other contributions were made on this subject.

The next main theme discussed was fluid and electrolyte balance in obstetrics and gynaecology. A particularly fine review of the present state of knowledge of the physiology and pathology of water and electrolytes during pregnancy was given by L. Heller and his paper contains an excellent bibliography.

The final symposium of the Conference was devoted to the problem of urinary incontinence in women. Professor Langreder of Mainz discussed the pathological anatomy of stress incontinence; his paper includes 303 references. The diagnosis, with particular reference to urethrocystography, and the treatment of stress incontinence of urine were then reviewed.

In addition to the symposia many other contributions covering a wide range of obstetric and gynaecological practice were made. Schmidt and Kyank described their experiments with placental homogenate and demonstrated clearly the ability of the placenta to synthesize *in vitro* adreno-cortical steroids from progesterone. Dr. Shettles of New York demonstrated the results of his studies of the living human ovum using the phase contrast microscope. The papers mentioned give some idea of the variety of subjects discussed at what must have been a stimulating and well-organized Conference, but which must have demanded an indefatigable intellectual digestive system.

Peter J. Huntingford

"Cancer of the Cervix: Diagnosis of Early Forms." Ciba Foundation Study Group, No. 3. Edited by G. E. W. WOLSTENHOLME and M. O'CONNOR. Pp. 114, with 27 illustrations. J. & A. Churchill Ltd., London, 1959. Price 12*s*. 6*d*.

AN adequate review of this small volume would entail almost a précis of a book of few more than 100 pages: it would be better for every gynaecologist and every pathologist who examines gynaecological material to read it for himself. The book contains 7 papers read by authors from Bonn, Cardiff, Cologne, Harvard, Paris, Stockholm and Zurich at a one-day conference held in London in May, 1959. Problems of definition, classification, histo- and cyto-pathology, detection and treatment were aired, and the views of the speakers were subjected to the cut and thrust of discussion. A suggested revision of the present staging of cervical cancer and a review of the modes of treatment of carcinoma *in situ* were but two of the clinical features discussed. Conservative treatment of the pre-invasive lesion demands indefinite follow-up of the patient. Some might hold that, although such a policy might save an unnecessary hysterectomy, this physical gain to the woman might be more than offset by the mental strain to which she is subjected.

"A Textbook of Human Embryology." By R. G. HARRISON, M.A., D.M., Derby Professor of Anatomy in the University of Liverpool. Pp. xi+244. Blackwell Scientific Publications, Oxford, 1959. Price 45*s*.

THIS book has been written by Professor Harrison at the request of his students, and is expressly intended for medical students. Those requiring further information or advanced training are given references to recent literature.

Students attending Professor Harrison's course will undoubtedly find it an excellent book when read in conjunction with his lectures. Others will find it insufficient in places, and the emphasis is rather unevenly distributed. In a book of 220 pages for medical students,

it would seem unnecessary to devote 13 pages to the normal gross anatomy of the male reproductive system, including 6 illustrations of the blood supply and drainage of the testis and prostate and 3 of the structure of the inguinal canal. There is, on the other hand, no clear definition or description of the mitosis or meiosis, and words like haploid and diploid are used without introduction or definition.

There are some inaccuracies in the index. References in the index to liver, for example, take the reader to pituitary gland on p. 47, teeth on p. 90 and midgut on p. 109. Also, among the 21 other references to liver, none gave a clear-cut description in one place of the development of the liver and its adnexa as such.

Abnormalities are not dealt with in sufficient detail for a medical student, to whom they can be very important. None, for example, is mentioned for the bile ducts; those of the ureter are, in the opinion of the reviewer, inadequately described, and it is disappointing to find a median cleft of the upper lip illustrated without reference to its infrequency.

There is an adequate description of implantation and the formation of the placenta, and a clear account of hormonal influences is given.

REVIEW OF CURRENT LITERATURE

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OBSTETRICS

81. Recent Advances in Gynaecology and Obstetrics in the U.S.S.R. (Din realizarile recente in doeniul Ginecologies et Obstetricii in U.S.S.R.)

By N. GHEORGNIN and I. ROMAN. *Obstet. Ginec.* (*Bucarest*). pp. 81–86. Jan.–Feb. 1959.

The authors attended the 10th International Congress of Gynaecology and Obstetrics in Moscow in December, 1957, and give a short report of the proceedings, by which they were evidently much impressed.

The Soviet Government has always been interested in the welfare of the mother and child, and has created special privileges for the expectant mother, including increased leave from work, of between 16 and 18 weeks. There has been a great improvement in the health of mothers and children compared to that of pre-revolution days. They now have a maternal mortality of 0·07 per cent, and a foetal mortality of 1·77 per cent. There are 143,000 obstetric beds and over 58,000 gynaecological beds, as well as 24,000 beds in nursing homes. With the development of this branch of medicine the number of gynaecologists and obstetricians has increased to 22,000.

The authors greatly admire the work they have seen in the Soviet Union. They mention the method of Nikolevi and Leghencenko for the treatment of asphyxia neonatorum, and the psycho-prophylactic method of analgesia for labour introduced by Velvorski.

Professor Hmeleveski treats intra-partum asphyxia by giving the mother vitamins B_1, C and P, and oxygen. If the foetal heart still remains irregular after 5 minutes of this treatment operative delivery is effected. For the treatment of asphyxia neonatorum Professor Persianinov injects a hypertonic solution of calcium chlorate (3 ml. of 10 per cent solution) and glucose (7 ml. of 40 per cent solution) into the umbilical artery under high pressure. He claims that this has a neuro-reflex action which improves cardiac activity and establishes respiration. The authors have used this method and the neonatal deaths from asphyxia have been reduced from 2·7 to 1·2 per cent.

Professor Petcenko and Dr. Demicev have designed a vacuum extractor for use in cases of hypotonic uterine inertia with malposition of the head, which effects rotation of the head in a physiological manner, and results in a natural expulsion of the baby, with a reduction in the number of forceps deliveries. These authors also use oxygen very freely, giving it to the mother in cases of intra-partum asphyxia and even as a prophylactic in normal labour. If the baby is born with blue asphyxia they recommend leaving the umbilical cord uncut until the vessels have stopped pulsating and the baby cries. Meanwhile oxygen is given to the mother. In cases of white asphyxia the same method is followed, but the baby is also given artificial respiration with special equipment. They claim that this has reduced the neonatal mortality rate from 9 to 0·6 per cent. Thermostatically controlled oxygen incubators are used.

To relieve pain in labour Soviet obstetricians use the psycho-prophylactic type of analgesia, which they believe helps to prevent miscarriages, premature labour, and inco-ordinate uterine action in labour. Lectures are given throughout pregnancy on anatomy and physiology, abortion, sexual hygiene, the nervous system, diet,

clothing, care of the skin and breasts, and physical exercises are taught. They are also told about the Soviet laws relating to the care of mothers and children. The confidence of the patients is gained and thus fear of labour is prevented. When the psycho-therapeutic method is not successful, analgesic drugs are given. They have also noted that hypotensive drugs accelerate labour.

In the gynaecological sphere Professor Mihailov stresses the importance of early diagnosis and treatment of the pre-cancerous condition, and discusses the use of surgery combined with radiotherapy for carcinoma. In order to avoid ureteric fistulae during Wertheim operations the ureters are isolated and wrapped in freshly obtained amniotic membrane. By this method the incidence of fistulae has been reduced from 9·3 per cent to 2·2 per cent.

In the prophylaxis of genital cancer, any woman who attends an out-patient department is first examined by a trained nurse, who inspects her cervix with a speculum. If the nurse is satisfied that there is no abnormality she will then refer the patient to the department originally asked for. By this procedure the number of stage III cases of cervical cancer was reduced by 10 per cent.

With a wide experience of surgical treatment of cervical cancer the mortality rate has been reduced from 3 to 1·5 per cent.

In functional menorrhagia gynaecologists recognize that there may be many causes, psychological, endocrine, infective or hepatic. Because of the large number of women with hormonal and inflammatory conditions, clinics for paediatric gynaecology have been organized.

The Soviet Union has started Birth Control Clinics because of the many complications following spontaneous and induced abortion, and they are now using a spermo-absorbant devised by V. Slonitiki which has proved very effective. For the first time in the U.S.S.R. they have organized institutes for research in connexion with physiology and pathology in women. In Gruzia Professor Jordania is running an institute for the study of problems related to the development of the foetus and the diagnosis and treatment of infertility. This institute also deals with marital difficulties. It has about 50 beds and a polyclinic, and anyone may seek advice on marital problems.

Sylvia Lerer

PREGNANCY

82. **Potassium/Calcium Quotient and the Autonomic Balance during Pregnancy.** (Kalium/Kalzium-Quotient und vegetative Reaktionslage während der Gestation.)

By C.-J. Ruck. *Zbl. Gynäk.*, **81**, 1809–1816. Nov. 14, 1959. 2 tables. 2 figs. 52 refs.

The author determined the quotient between the potassium and the calcium serum levels in 1,113 cases (83 non-pregnant women, 733 pregnant, 50 in labour and 247 in the puerperium). The ratio was found to be constant in the non-pregnant, during the first 6 months of pregnancy and in the puerperium, whereas the quotient rises from the seventh month towards term. The normal quotient is given as 2·00, and the increase observed during the third trimester of pregnancy amounted to 6 to 8 per cent. This is due to a rise in the potassium and a decrease in the calcium levels in the serum.

The author regards this finding as indicating a relative predominance of the sympathetic nervous system after the sixth month of pregnancy.

Bruce Eton

83. **Observations Regarding the Duration of Pregnancy on the Basis of Basal Temperature Records.** (Beobachtungen über die Dauer der Schwangerschaft mit Hilfe der Basaltemperaturmessung.)

By K. Knörr and V. Probst. *Zbl. Gynäk.*, **81**, 1742–1747. Oct. 31, 1959. 2 tables. 2 figs. 6 refs.

The authors arranged for 101 women to record their waking temperature before and during pregnancy. Eleven women miscarried and 69 had been delivered up to the time of writing. Duration of pregnancy in the case of mature children varied between 241 and 286 days after conception. The average duration was 265 to 266 days. However, most of these patients had been attending the infertility or endocrine clinics. Irregular cycles were common amongst them, which explains the occurrence of cases of conception on the 33rd, 34th, 45th and 83rd days of the cycle. There were 6 cases of genuine prolonged pregnancy which exceeded the average duration of pregnancy by more than 14 days.

Bruce Eton

84. **Behaviour of the Cervix in Cases of Prolonged Pregnancy.** (Über das Verhalten der Cervix uteri bei der übertragenen Schwangerschaft.)

By A. Dzioba and F. Drabina. *Zbl. Gynäk.*, **81**, 1632–1635. Oct. 10, 1959. 22 refs.

The authors review a series of 52 patients whose pregnancy had exceeded 42 weeks. In the first group of 11 primigravidae and 17 multigravidae the external os admitted 1½ to 3 fingers and the internal os 3 to 4 fingers. In the second group, consisting of 12 primigravidae and 12 multigravidae, the external os was closed or barely admitted one finger and the internal os was rigid and not more than one finger dilated. Amongst the 17 multigravidae of the first group labour began within 8–24 hours after vaginal examination, with the exception of one patient. The findings were similar amongst primigravidae in this group. In the second group labour did not start until one to 3 weeks later, but in the majority of these patients signs of maturity of the cervix developed during that time.

Bruce Eton

85. **Tranquilizer Interference in the Rana Pipiens Chorionic Gonadotrophin Test.**

By J. R. Brillhart. *Obstet. and Gynec.*, **14**, 581–587. Nov. 1959. 2 tables. 27 refs.

A number of non-pregnant patients on tranquillizer drugs had their urine tested for chorionic gonadotrophins

using the *Rana pipiens* frog test. Promazine and chlorpromazine gave false positive frog tests in 24 per cent and 18 per cent respectively of the patients studied. Other phenothiazine derivatives induced no false positive tests.

Investigation of promazine sulfoxide, a metabolite of promazine, failed to show that it was the cause of the false positive test. Phenothiazines given to pregnant women may cause false negative frog tests. Using the mouse or rabbit pregnancy test instead of the frog test, the results were found to be quite reliable. *J. G. Dumoulin*

86. **Protoveratrine in the Treatment of Hypertension During Pregnancy.**

By H. M. Carey. *N.Z. med. J.*, **58**, 467–479. Aug. 1959. 3 tables. 3 figs. 8 refs.

Protoveratrine has been used intravenously, subcutaneously and by mouth to treat cases of hypertension during pregnancy. Intravenous infusion was used mainly when rapid and accurate control of the blood pressure was required. Once the hypertension had been controlled in this way the blood pressure level was usually maintained by intermittent subcutaneous injections. In less urgent cases administration was commenced by subcutaneous injections. Oral protoveratrine was usually given to patients admitted to hospital before the 35th week of pregnancy with a basal diastolic pressure consistently above 100 mm. of mercury. Reserpine was usually administered with protoveratrine to potentiate the hypotensive action, but no clear-cut evidence of its value was obtained. Labour was induced between the 34th and 36th weeks by rupture of the membranes, followed, if necessary, by a pitocin drip. Occasionally Caesarean section was necessary. Once the patient was transferred to the labour ward for surgical induction, subcutaneous administration replaced oral protoveratrine.

Reductions of basal diastolic pressure readings of up to 30 mm. of mercury were sustained for short periods by parenteral administration, while a reduction of 20 mm. of mercury has been sustained for long periods by oral administration. The results were obtained without troublesome side effects. There was no evidence in the present small series of cases that this treatment improved the foetal salvage. *L. Woodrow Cox*

87. **The Assessment of the Risk of Intra-Uterine Death in Pre-eclampsia.**

By H. M. Carey and A. W. Liley. *N.Z. med. J.*, **58**, 450–460. Aug. 1959. 11 tables. 1 fig. 16 refs.

All cases of pre-eclampsia admitted to the National Women's Hospital, Auckland, in the years 1954–57 were studied. One hundred and sixty-five women were admitted prior to the last month of pregnancy; amongst these were 39 intra-uterine deaths of the foetus. An attempt was made to analyze the relationship between the intra-uterine death rate and the duration of pregnancy at the onset of pre-eclampsia, the severity of hypertension and the severity of proteinuria. It is concluded that the intra-uterine death rate is more dependent on the duration of pregnancy at the onset of pre-eclampsia than on the level of either diastolic pressure or protein excretion. It is suggested that earlier, rather than later, intervention gives a better hope for saving babies which are likely to die *in utero*. The difficulty of recognizing individual cases with placental insufficiency is recognized.

L. Woodrow Cox

88. **Hydatidiform Mole Complicated by Eclampsia.**

By S. Post. *Amer. J. Obstet. Gynec.*, **78**, 878–880. Oct. 1959. 7 refs.

The patient, a primigravida, aged 22 years consulted her medical attendant for the first time at the eighth week of pregnancy when she complained of "intermittent spotting" noticed during the previous 4 weeks.

The uterus was the size of an 8-week pregnancy, a frog pregnancy test was positive, the blood pressure was 120/80, and the urine was clear. Three weeks later she complained of nausea and occasional vomiting, and the intermittent bleeding had continued. The uterus had grown rapidly and was now the size of a 14-weeks pregnancy. A molar-pregnancy was suspected and instructions were given to save all tissue passed. Thirty-one days after the first visit, that is 87 days after the last menstrual period, the patient's husband reported that his wife had had a convulsion. She was immediately admitted to hospital. Her blood pressure was 170/110, pulse 100, and the urine contained 4 plus albumin. Sodium amytal was given intravenously and following this there was a second generalized convulsion. Thirty-six hours after this abdominal hysterotomy was done and a hydatidiform mole evacuated. When seen 3 weeks later she was well with normal blood pressure and urine. *F. J. Browne*

89. **The Problem of Contraception and Legalised Abortion in the U.S.S.R.** (Problema kontracepcii i organizacia bor'by a abortami w U.S.S.R.)

By K. Nikonchik. *Akuš. i Ginek.*, No. 6, 3–6. 1959.

Leading scientists in the U.S.S.R. are engaged in research and advice on the manufacture of contraceptives and their medical use in family planning. All degrees of personnel down to midwives and medical auxiliaries are trained to explain to the population at large the advantages and shortcomings of contraceptives.

The authorities pay substantial maternity benefits and grant maternity leave for 8 weeks before and 8 weeks after delivery. Lectures, films, pamphlets, brochures and every available means of spreading information are mobilized to promote good motherhood. Special medals and quotations are granted to distinguished mothers.

In March 1956 the U.S.S.R. revoked the law forbidding the induction of abortion. Statistics for the past 4 years show that though the number of miscarriages has increased the number of births has remained unchanged.

[The legislation is intended to allow a woman to decide for herself upon conception, abortion and motherhood.]

E. W. Collis

90. **Abnormal Size of the Internal Cervical Os and Tendency to Abortion.** (Abnorme Weite des Os internum und Neigung zu Aborten.)

By J. LINDAHL and C.-G. HELANDER. *Geburtsh. u. Frauenheilk.*, **19,** 1071–1075. Dec. 1959. 1 table. 29 refs.

The authors have followed the obstetric histories of 31 patients who had had a pregnancy terminated in the Karolinska Sjukhuset, Stockholm, and who were subsequently proven to have an abnormally wide internal cervical os. Each of these patients was examined after the termination by hysterosalpingography during the second half of the menstrual cycle, when this had been re-established. By direct measurement they were found to have an internal os measuring 5 mm. or greater (range 6–11 mm.), and in all cases free spill of the contrast medium was seen from at least one tube. None of these patients was subjected to any further vaginal surgery. In the 6 years following these investigations 17 women carried 25 pregnancies; in 16 of them there was no tendency to abortion. One patient, who had had two abortions at 12 and 24 weeks prior to her termination and hysterosalpingogram, went into labour prematurely on two occasions and then had a spontaneous abortion at 20 weeks (the internal cervical os measured 9 mm.). Three other patients had spontaneous miscarriages (all occurred at 12 weeks), but only after they had carried a pregnancy uneventfully to term following the measurement of the internal cervical os on a hysterosalpingogram. The authors conclude that an abnormally wide internal cervical os as measured on a hysterosalpingogram should not be regarded as evidence of a tendency to abortion or premature labour.

Peter J. Huntingford

91. **Some Observations on Threatened Abortions.**

By M. K. K. MENON, M. WILMOT and K. SOGHRABI. *J. Obstet. Gynaec. India*, **10,** 84–90. Sept. 1959. 5 tables. 5 refs.

A threatened abortion is defined as slight uterine bleeding with pain in the first twenty-eight weeks of pregnancy, the cervical os remaining closed. Consecutive cases were taken in which there was no known aetiological factor, and they were studied from the point of view of crystallization of cervical mucus, vaginal cytology and excretion of urinary pregnanediol.

One hundred and fifty-four patients who were random aborters were studied. It seemed that once ferning appeared in the cervical mucus in a case of threatened abortion over 80 per cent miscarried. If 30 per cent acidophils were present in a vaginal smear this too was of prognostic significance, as again 80 per cent miscarried. Abnormally low pregnanediol values appeared to be associated with oestrogenic vaginal smears and ferning of the cervical mucus.

The cases were divided into two groups. Cases in Group A (97 cases) were treated by bed rest, oral iron and sedatives, and 89 per cent aborted. Cases in Group B (57 cases) were treated similarly, but with the addition of 5 mg. stilboestrol orally twice daily, and 56 per cent aborted.

John McKiddie

92. **The Significance of "Clear Glands" in the Endometrium for the Diagnosis of Uterine Abortion and a Contribution on "Prolonged Shedding of the Endometrium".** (Die Bedeutung des "hellen Drüsen" im Endometrium für die Diagnose des uterinen Abortes. Zugleich ein Beitrag zur "verzögerten menstruellen Abstossung".)

By L. OVERBECK. *Geburtsh. u. Frauenheilk.*, **19,** 1098–1109. Dec. 1959. 3 tables. 5 figs. 22 refs.

In a previous article (*Geburtsh. u. Frauenheilk.*, 1959, **19,** 983) the author has described the significance of "clear glands" that are to be found in the endometrium of patients with tubal pregnancies (see abstract No. 101). Using the same classification he has studied the uterine curettings obtained from 373 cases of uterine abortion. In 256 cases remnants of pregnancy decidua were obvious. "Clear glands" were identified in 42 of 86 cases with curettings which showed advanced decidual degeneration. In 11 cases the uterine curettings showed a histological picture which is described as "prolonged shedding of the endometrium" or "mixed endometrium"; "clear glands" were present in 9 of these. In the remaining 20 cases the endometrium was in the interval (resting) phase, and in none of these were "clear glands" identified. Therefore, in the 117 cases in which pregnancy decidua was not in a good state of preservation "clear glands" were found in 51 (43·6 per cent); but in only 15 (12·8 per cent) was there no other evidence, such as placental villi, hyaline decidual remnants or hyalinization of blood vessels, suggestive of a preceding pregnancy. The author concludes that the presence of "clear glands", which he regards as remnants of the decidua spongiosa, are also to be found in the endometrium following uterine abortion, but that their diagnostic value is of less importance than those found in cases of ectopic gestation.

In addition, the author has studied the curettings from 1,568 patients in whom there was no clinical suspicion of pregnancy to determine whether the presence of "clear glands" in the endometrium might be pathognomonic of a pre-existing pregnancy. "Clear glands" were found in only 18 (1·2 per cent). With this information the records of these patients were re-examined, and in all of them a period of prolonged or irregular bleeding had followed a period of amenorrhoea of at least 5 weeks. The author believes that these 18 patients had all probably been pregnant. In 13 of this group the endometrium which contained the "clear glands" showed a picture of "prolonged endometrial shedding".

Dr. Overbeck continues by discussing the relationship of "prolonged shedding of the endometrium" and recently terminated pregnancies. He believes that the presence of clear glands is evidence in support of such a relationship. In conclusion he points out the similarity between his findings and those of Arias-Stella (*Arch. Path.*, 1954, **58,** 112), although the latter author has interpreted his findings in a different way.

Peter J. Huntingford

93. **The Anatomy and Pathology of Premature Separation of the Placenta.**

By I. E. VAN DEN ENDE. *S. Afr. med. J.*, **33**, 737–740. Sept. 5, 1959. 3 figs. 21 refs.

The author discusses implantation and the development of the foetal and maternal portions of the placenta. The foetal prognosis is much better in cases of placenta praevia in which the marginal sinus is chiefly involved than in cases in which the central area of the placenta is separated. The features of marginal sinus rupture are described. An attempt is made to correlate the pathological findings in premature placental separation and in pre-eclampsia. However placental infarcts occur in about 60 per cent of normal placentae at term. Hertig demonstrated morphological evidence of acute atheromatous changes in decidual arterioles with fibrinoid degeneration of the intima. Dixon and Robertson (*J. Obstet. Gynaec. Brit. Emp.*, 1958, **65**, 803) obtained specimens of the placental bed at Caesarean section. They found vascular changes in the decidual and myometrial vessels in patients with pre-eclampsia and hypertension similar to those usually found in systemic hypertension. The changes are directly related to the clinical severity of the condition. Histological sections taken from a 19-year-old primigravida with severe pre-eclampsia are shown. J. T. Louw suggests that, as pre-eclampsia is not seen in association with chorion epithelioma, it is the decidual change which may provide the clue to the aetiology of pre-eclampsia.

L. J. Abramowitz

94. **Folic Acid Deficiency in Pregnancy. The Pathogenesis of Megaloblastic Anaemia of Pregnancy.**

By I. CHANARIN, B. M. MACGIBBON, W. J. O'SULLIVAN and D. L. MOLLIN. *Lancet*, **2**, 634–639. Oct. 24, 1959. 5 tables. 4 figs. 40 refs.

This paper from the Postgraduate Medical School of London reports an investigation into folic acid deficiency in normal pregnancy, twin pregnancy and pregnancy complicated by megaloblastic anaemia. Two methods of study were used to assess folic acid deficiency:

(1) The rate of clearance of folic acid from the plasma following an intravenous injection of 15 microgrammes of folic acid, the serum concentration being measured 3, 15 and 30 minutes after injection ("the folic acid clearance test").

(2) The serum folic acid level 1 and 2 hours after an oral dose of 40 microgrammes of folic acid was measured. The subject was previously "saturated" with folic acid by giving 15 mg. intramuscularly daily for four days, the test being carried out 36 hours later ("the folic acid absorption test").

The folic acid content of the serum in both tests was measured by microbiological assay using *Streptococcus faecalis* as the test organism.

Folic acid clearance tests were carried out on 30 non-pregnant female controls, 250 pregnant women without anaemia, 11 patients with normal twin pregnancy and 11 patients with untreated megaloblastic anaemia, diagnosed by sternal marrow aspiration. It was found that the rate of clearance of folic acid from the plasma was increased in two-thirds of pregnant subjects in late pregnancy and in all patients with twin pregnancy. The most rapid rate of clearance was found in those patients with megaloblastic anaemia.

Folic acid absorption tests were carried out on 90 healthy subjects of both sexes, 45 pregnant women between 20 and 40 weeks, and 10 women with treated megaloblastic anaemia in pregnancy. The peak serum folic acid concentration was significantly lower in the pregnant than in the non-pregnant patients, whilst the patients with megaloblastic anaemia showed significantly lower levels than those found in the other pregnant patients.

The authors conclude that there is an increased demand for folic acid in pregnancy and especially in twin pregnancy. This, coupled with an impaired absorption of folic acid, may lead to a folic acid deficiency. Where the deficiency is severe, megaloblastic anaemia may develop. The absorption of folic acid is most impaired in patients with megaloblastic anaemia and this may contribute to the severe degree of folic acid deficiency found in these patients.

[The early diagnosis of megaloblastic anaemia of pregnancy may be difficult even after sternal marrow aspiration. There would seem to be some justification for giving folic acid to any case of iron resistant anaemia in pregnancy. Providing the therapy is discontinued immediately post-partum the risk of masking the rare case of true pernicious anaemia complicated by pregnancy is very slight.]

J. M. Brudenell

95. **A Preliminary Study on the Incidence of Occult Blood in the Stools in Pregnancy.**

By H. O. DICKENS and M. V. PLANAS. *Amer. J. Obstet. Gynec.*, **78**, 864–867. Oct. 1959. 3 tables. 3 refs.

A 35-year-old gravida-5 with severe anaemia at the 5th month was found to have 4 plus occult blood in her stools for which no cause could be found, and which disappeared after delivery. This case prompted a study to determine the frequency of occult blood in the stools during pregnancy. A total of 58 women were included—14 primigravidae and 44 multigravidae. Of 30 women between the ages of 15 and 25, 8 showed 4 plus occult blood in the stools, 1 showed 2 plus and 1 showed 1 plus. In the age group 25 to 35 there were 22 women, 7 of whom showed 4 plus blood, 1 showed 2 plus and 2 showed 1 plus. Among the 3 patients in the 36–45 age group only 1 had 4 plus occult blood. The incidence was therefore the same in all the age groups—about 36 per cent. All patients with haemoglobin of 8·5 g. per cent or under showed occult blood. No intestinal parasites were found in any patient. After elimination of all possible causes the authors conclude that the most plausible explanation is the pelvic congestion accompanying pregnancy.

F. J. Browne

96. **Prophylactic Isoniazid. Protection of Infants in a Tuberculosis Hospital.**

By B. A. DORMER, I. HARRISON, J. A. SWART and S. R. VIDOR. *Lancet*, **2**, 902–903. Nov. 21, 1959.

This paper, from the King George V Hospital, Durban, South Africa, reports the results of the prophylactic administration of isoniazid to infants born to Bantu mothers with active tuberculosis. Before the present regime was started infants born to tuberculous mothers were separated immediately from their mothers and sent to other institutions, relatives or foster parents. Under this system in a primitive community it was found that the care of separated infants was often inadequate and a high proportion died of gastro-enteritis associated with artificial feeding. It was therefore decided to keep the babies born in hospital with their mothers, encourage breast feeding and at the same time to administer prophylactic isoniazid. The dose of isoniazid used was 25 mg. twice daily for the first six months and thereafter 50 mg. twice daily.

In 98 children born to tuberculous mothers there were no cases of tuberculosis and where the isoniazid was given regularly the Mantoux test remained negative. No adverse effects were noted in the mothers. *J. M. Brudenell*

97. **Maternal Influenza and Congenital Deformities.**
By V. P. Coffey and W. J. E. Jessop. *Lancet*, **2**, 935–938. Nov. 28, 1959. 6 tables. 14 refs.

The authors carried out a prospective study of the effects of influenza during pregnancy on the occurrence of congenital foetal abnormality. In all, 669 patients who attended the antenatal clinics at the Rotunda, National Maternity and Coombe hospitals, Dublin, during the period 1st October, 1957 to 1st October, 1958 answered in the affirmative to the question "Have you had influenza during this pregnancy?" A similar series of controls were chosen from the patients who had not had influenza. (The authors timed the start of the investigaton to coincide with the arrival in Ireland of the Asian influenza pandemic.)

It was found that the incidence of congenital deformity in the offspring of mothers who had had influenza during pregnancy was more than double the incidence in the control group, a statistically significant difference. Most of the abnormalities noted were of the central nervous system, anencephaly being the commonest. When the effect of the stage of pregnancy at which the attack occurred was studied, it was found that the risk of deformity was greatest when the infection occurred during the first three months. Thereafter the risk declined during the two subsequent trimesters. No difference was found in the incidence of prematurity and stillbirth between the two groups and the sex ratio of the children was the same.

In considering the effect on the offspring of an attack of influenza during the first trimester the authors estimate the risk of congenital foetal deformity as being more than 7 per cent. In view of this figure they recommend that serious consideration should be given to affording protection by vaccination to women in early pregnancy when an influenza epidemic is in progress.

The authors conclude by discussing the possible ways by which a virus can damage the embryo.

J. M. Brudenell

98. **Pelvic Inflammatory Disease in Pregnancy.**
By S. Friedman and M. L. Bobrow. *Obstet. Gynec.*, **14**, 417–425. Oct. 1959. 42 refs.

Acute Purulent Salpingitis in Late Pregnancy.
By M. Lancet and A. Cohen. *Obstet. Gynec.*, **14**, 426–428. Oct. 1959. 6 refs.

In the first of the above two papers 2 cases are described in which laparotomy was carried out during pregnancy (at 6 weeks and 28 weeks) and a unilateral ovarian abscess was found. A further 3 cases are described in which the presumptive diagnosis was pelvic peritonitis during pregnancy, and certainly in 2 of these criminal interference produced the infection without causing abortion. Whereas salpingitis during pregnancy seems to be due to criminal interference, ovarian and tubo-ovarian abscesses are not always due to attempted abortion; other aetiological causes can be pre-existing post-abortal or post-partum inflammatory disease, blood stream infection from a distant focus, lymphatic spread from an infected cervix, and infection in an ovarian cyst.

The authors state that acute gonococcal salpingitis or a flare-up of a chronic gonococcal infection rarely, if ever, occurs during a pregnancy.

In the second paper a case of unilateral right-sided salpingitis in the sixth month of pregnancy is described in which salpingectomy was followed by abortion.

J. G. Dumoulin

99. **Hypothermia and Hypotension During Craniotomy in a Pregnant Woman.**
By F. Wilson and C. B. Sedzimir. *Lancet*, **2**, 947–949. Nov. 28, 1959.

A patient who was 32-weeks pregnant had a spontaneous intracranial haemorrhage from a congenital "berry" aneurysm. Urgent craniotomy under hypothermia and hypotension was performed, enabling the aneurysm to be clipped close to its neck. The hypothermia and hypotension were associated with considerable uterine hypertonicity and excessive foetal movements. The patient went into labour 29 hours after the operation and gave birth to a living premature infant which survived. Apart from some residual dysphasia the mother made a complete recovery.

The authors discuss the effects of hypothermia and hypotension on uterine tone and haemodynamics.

J. M. Brudenell

100. **Fetal Death in Utero.**
By J. A. Pritchard. *Obstet. and Gynec.*, **14**, 573–580. Nov. 1959. 4 tables. 4 figs. 7 refs.

Measurements of plasma fibrinogen were made in more than 100 women with a dead foetus *in utero*. Observations indicate that such patients are most unlikely to develop dangerous hypofibrinogenaemia in less than 5 weeks after foetal death. After that, however, the odds are 1 in 4 that they will do so. If hypofibrinogenaemia develops, it is most likely to do so gradually.

It may be asymptomatic before delivery, or there may be gingival bleeding or ecchymosis. After it develops it will probably persist until the uterus is emptied. Fibrinogen administered without emptying the uterus results only in a transient elevation of the level of circulating fibrinogen, and in using it there is the danger of homologous serum hepatitis. Labour does not result in further fibrinogen depletion.

It is obviously wise not to allow a patient to go for longer than 3 or 4 weeks with a dead foetus in the uterus.

J. G. Dumoulin

101. **The Significance of "Clear-glands" in the Endometrium in the Diagnosis of Tubal Gestation.** (Die Bedeutung der "Hellen Drüsen" im Endometrium für die Diagnose der Tubargravidität.)

By L. OVERBECK. *Geburtsh. u. Frauenheilk.*, **19**, 983–991. Nov. 1959. 2 tables. 6 figs. 34 refs.

The author has studied the uterine curettings from 100 cases of ectopic pregnancy treated in the University Gynaecological Clinic of Marburg/Lahn. According to the histological appearances he has divided them into 6 groups:

(1) Fully functional decidua (22 cases).

(2) Degenerating decidua, which is further subdivided into three stages: First stage: The decidual stroma is intact, but the glandular epithelium is shrinking and regressing (33 cases). Second stage: Irregular shrinkage of both stroma and glands, giving a patchy structure (18 cases). Third stage: An almost uniform shrinkage of the decidua giving the appearance of a functionless endometrium (15 cases).

(3) The onset of a new endometrial cycle. (*a*) With patchy but recognizable elements of the 3rd stage of decidual degeneration (7 cases). (*b*) With no remaining evidence of decidua (5 cases).

The first two groups allowed a definite diagnosis of the presence of a pregnancy to be made. In the other groups the diagnosis was more difficult. But the author noted in many cases the presence of characteristic "clear glands", which he believes are evidence of a previously existing pregnancy and that they represent remnants of glands of the decidua spongiosa. Using periodic acid Schiff reagent these glands were shown to contain glycogen. The cytoplasm of the "clear glands" was vacuolated and the cell nuclei were polymorphic and pyknotic. Such "clear glands" were recognizable in 88·9 per cent of those cases classified as the 2nd stage of decidual degeneration; in 66·7 per cent of those in the 3rd stage; and in 57·1 per cent of those in which a new endometrial cycle had begun. "Clear glands" were present in 30 of the 45 (66·7 per cent) cases in which a decidual reaction of the stroma was no longer recognizable. The author points out that these "clear glands" (hellen Drüsen) are to be distinguished from the "clear cells" (hellen Zellen) of Feyrter and the "cellules claires" of Angel and Wittig.

Peter J. Huntingford

102. **The Early X-ray Diagnosis of Ectopic Pregnancy.**

By N. V. MARTOVA and A. CYCULOSKU. *Akuš. i Ginek.*, No. 4, 75–77. July 1959. 6 tables. 2 refs.

A pneumoperitoneum with oxygen was used to investigate the pelvic organs. With the patient in Trendelenburg's position a needle (6–8 cm. long) is inserted into the peritoneal cavity midway between the umbilicus and the left anterior iliac spine. Six hundred to 1,000 ml. of oxygen is then inserted at a speed of 100 to 150 ml. per minute. The patient is turned on to her abdomen. The X-ray tube beam is directed to the last coccygeal vertebrae at an angle of 45 to 50 degrees from the horizontal. An antero-posterior and two lateral photographs are taken.

The shadow of the uterus with ectopic pregnancy is usually larger than the one of a normal non-pregnant uterus. An affected uterine cornu is enlarged; its border is distinctly shaped. A tube containing an ectopic pregnancy is thickened and elongated.

The X-ray exposure must not exceed 1·5 r.; this seems quite adequate to get a reasonably readable photograph.

[In cases on the verge of rupture the pneumoperitoneum might precipitate this.]

E. W. Collis

103. **Early Diagnosis of Multiple Pregnancy.**

By C. A. NOVOTNY, W. K. MASS and D. A. CALLAGAN. *J. Amer. med. Ass.*, **171**, 880–884. Oct. 17, 1959. 6 figs. 8 refs.

The early diagnosis of multiple pregnancy is desirable because of the associated complications. Because of the growing concern for irradiation hazards the authors decided to investigate the use of the electroencephalograph to detect the presence of multiple foetal hearts. At the U.S. Naval Hospital, Portsmouth, Virginia, 321 tracings were obtained from 295 patients. The stage of pregnancy is important, and the earliest positive diagnosis of twins was made at 16 weeks. The most favourable period was after the 20th week when the diagnosis was made without a single error. At this hospital the test is now made as a routine in all cases of suspected multiple pregnancy or intra-uterine death. The electroencephalograph is safe and accurate for this purpose and could be used more widely. The test is easily performed by a trained technician.

D. W. James

LABOUR

104. **The Optimal Time for Induction in Pre-eclampsia.**

By H. M. CAREY and A. L. LILEY. *N.Z. med. J.*, **58**, 460–466. Aug. 1959. 5 tables. 11 refs.

The foetal mortality at each week of gestation was recorded in 165 pregnancies which developed pre-eclamptic signs before the 36th week. In the same hospital the foetal mortality due to prematurity and the complications of prematurity was also recorded at each week of gestation. The suggestion is made that as soon as the calculated risk of intra-uterine foetal death appreciably

exceeds the risk of neonatal death due to prematurity, the pregnancy should be terminated.

L. Woodrow Cox

105. **Induction of Labour with Oestradiol Monobenzoate.** (Sul 'impiego del monobenzoato di estradiolo (Ovociclina M) nel determinismo del travaglio di parto.)

By A. Finotti and U. Citti. *Minerva ginec. Torino*, **11**, 738–744. Sept. 30, 1959. 3 tables. 72 refs.

Follicular hormone in adequate quantity is regarded as essential for the sensitizing of the uterine musculature, especially as regards its bipolar co-ordinating action in the normal process of labour under the activating action of pitocin. In place of using water-soluble preparations of oestrogens which are quickly absorbed and of short action, the authors used a micro-crystalline preparation of oestradiol monobenzoate in a single injection of 20 mg. (two phials of Ovocyclin-M) which is stated to give a uniform level of the hormone lasting many hours. It was used in 15 cases of primary uterine inertia, 15 of secondary inertia, and 30 of postmature prolongation of pregnancy. Satisfaction is expressed with the results, especially in secondary inertia, and details are recorded.

[The idea appears physiologically sound, but no indication is given as to the effects on the function of lactation.]

W. C. Spackman

106. **Maturity of the Cervix as a Guide to Induction of Labour in Cases of Prolonged Pregnancy.** (Die Reife der Zervix als Anzeichen zur Einleitung der Geburtstätigkeit bei übertragenen Schwangerschaften.)

By A. Dzioba. *Zbl. Gynäk.*, **81**, 1627–1631. Oct. 10, 1959. 1 fig. 27 refs.

The author, after mentioning the physical signs of a "ripe" cervix, reports on a study of a series of patients whose pregnancy had progressed at least 14 days beyond the expected date of delivery, in whom there was no doubt about the accuracy of the date. He observed that the signs of a ripe cervix were absent in 23 out of 50 primigravidae and in 13 out of 52 multigravidae. He investigated the response of the uterus in these patients to oxytocin, administered as an intravenous drip after preliminary treatment with oestradiol. The more dilated the cervix was at the time of the initial vaginal examination the more readily did labour begin and the shorter was its duration. The author considers that whenever the cervix is unfavourable drug induction should not be carried out but that the cervix should be re-examined a week later.

[The author fails to supply details of the effects of his suggested routine on foetal mortality.]

Bruce Eton

107. **Diagnosis of Rupture of the Foetal Membranes by Detection of the Crystals in Vaginal Smears.** (Diagnostika otchozdienia okoloplodynch wod putoim opredie lenia krystalow w natiwnom mazkie.)

By O. P. Tarasenko and L. P. Pilcer. *Akuš. i Ginek.*, No. 6, 50–60. 1959. 5 tables. 5 refs.

Vaginal fluid suspected of being amniotic in origin is collected with a sterile pipette and transferred to a slide; the latter is then dried in the air or over an electric bulb. Under the microscope or even with a good magnifying glass crystals derived from amniotic fluid resembling branches of a fir tree can be clearly seen. The absence of these crystals is an indication that the foetal membranes are intact.

These findings were confirmed in 1,956 smears and the authors conclude that this test is accurate in 98 per cent of cases.

E. W. Collis

108. **A New Method of Accelerating Labour.** (Ein neuer Weg zur Verkürzung der Geburt.)

By G. Link. *Zbl. Gynäk.*, **81**, 1729–1742. Oct. 31, 1959. 8 tables. 5 figs. 43 refs.

The author reports the results of using a spasmolytic drug 1-(3, 4-Dimethoxyphenyl) - 1 - dimethylamino - 4 - phenylbutan-hydrochloride ("Monzal"). The drug acts directly on smooth muscle fibres and not on the autonomic nervous system. Tocographic records showed that its action on the uterus in labour consisted in lowering the basic tone, and in increasing the amplitude and often the frequency of contractions. The routine treatment for each patient consisted of a hot bath, application of a heated "belt" (in order to maintain the stimulating effect of warming the body), artificial rupture of membranes, and finally intramuscular injection of "Monzal".

Amongst 1,050 women thus treated the total length of labour varied from 1 to 7½ hours (512 primigravidae and 538 multigravidae). The average second stage lasted 17 minutes. No oxytocic drug was used in this series until after delivery.

Bruce Eton

109. **Incompetent Os of the Cervix as a Cause of Foetal Loss.**

By E. S. Taylor and R. H. Hansen. *J. Amer. med. Ass.*, **171**, 1312–1315. Nov. 7, 1959. 1 fig. 7 refs.

At the Colorado General Hospital this condition was found to occur not more than once in 500 pregnancies and the authors record the results of surgical treatment in 40 cases.

The diagnosis is suggested by recurrent middle trimester foetal losses, and previous trauma was a factor in one-half of the cases. Hysterographic confirmation is not necessary, although it is useful in excluding uterine anomalies. The painless passage of a 7 mm. Hegar dilator through the internal os of the cervix when the patient is not pregnant is presumptive evidence of cervical incompetence. It is important to observe the suspected cervix during pregnancy. The patient who has an incompetent cervix will demonstrate cervical effacement and dilatation starting between the 14th and 20th week of pregnancy.

If there is also deep laceration of the cervix this must be repaired by trachelorrhaphy when the patient is not pregnant, otherwise the Shirodkar type of operation is likely to fail. For correcting the incompetence the authors use a purse string type of ligature made of Mercilene

tape 8 mm. wide. The success rate was 80 per cent, 32 patients in this series of 40 cases treated surgically had normal full-term infants. Ten were delivered per vaginam after removal of the purse string and 22 had Caesarean sections. The advantage of Caesarean section is that the repaired internal os can be left intact for further pregnancies.

D. W. James

110. **The Danger of Uterine Rupture Following Normal Labour Which was Preceded by Caesarean Section.** (Die gevaar van uterusruptuur na keisersnee gevolg deur normale kraam.)

By P. M. BREMER. *S. Afr. med. J.*, **33**, 744–747. Sept. 5, 1959. 1 table. 26 refs.

About 30–45 per cent of patients who have had a Caesarean section are delivered *per vaginam*. Are the dangers of rupture increased after successful vaginal delivery? Eastman states that in 20 per cent of the cases of uterine rupture following Caesarean section there is a history of vaginal delivery following the section. Three cases are presented. The management of a second delivery following Caesarean section is discussed. The previous obstetrical history, the indications for and the type of operation are important, as is the nature of the puerperium. Other factors discussed are the state of the cervix, the size and presentation of the foetus and the uterine scar. In 40 per cent of cases rupture occurs without any obvious warning. Uterine rupture occurs in about 1 per cent of cases following lower segment Caesarean section. The perinatal mortality is generally 1 per cent higher after Caesarean section than it is with vaginal delivery. As long as these figures remain valid it is not necessary to perform elective Caesarean section as it is after classical Caesarean section. Pregnancy following previous uterine rupture is also discussed.

L. J. Abramowitz

111. **The Placental Transmission of Barbiturates and Thiobarbiturates and Their Pharmacological Action on the Mother and the Infant.**

By C. E. FLOWERS. *Amer. J. Obstet. Gynec.*, **78**, 730–740. Oct. 1959. 6 tables. 9 figs. 24 refs.

This is a study of barbiturates (nembutal, seconal and barbital sodium) and thiobarbiturates (pentothal, surital and neraval) with particular reference to their rate of transfer across the placenta, the time necessary to achieve equilibrium between the maternal and foetal blood, and their effect on the time required by the infant to establish respiration. Neither pentothal, surital nor neraval seemed to have any effect on the maternal or foetal arterial or venous oxygen saturation. All the barbiturates and thiobarbiturates pass rapidly across the placenta by simple diffusion, so that equilibrium between maternal and foetal blood content is achieved in 2 to 3 minutes. All the infants breathed immediately and showed no real depression after delivery. Thiobarbiturates have a rapid but transient hypnotic effect because of their high lipid solubility and affinity for body fat and tissues; equilibrium between brain and plasma is achieved in seconds, and there is no delay in their clinical action as in the case of seconal, nembutal and sodium barbital. These three drugs, however, disappear relatively slowly from the circulation and so maintain their pharmacological action for a long period of time. The contrast between the deep anaesthesia of the mother and the alertness of the infant may be due to the facts that the barbiturates and thiobarbiturates have a high lipid and low water solubility, and that the water content of the child's brain is higher than that of the mother.

F. J. Browne

OBSTETRIC OPERATIONS

112. **Caesarean Section Scar Safety.**

By L. O. S. POIDEVIN. *Brit. med. J.*, **2**, 1058–1060. Nov. 21, 1959. 8 figs. 14 refs.

A new method of assessing the soundness of lower segment Caesarean section scars is described. It involves hysterography and is therefore only applicable in the non-pregnant state.

All the cases examined (43) showed some deformity on the lower anterior uterine wall at the site of the scar which contrasted with the smooth contour seen in the 13 control cases who had had vaginal deliveries. Typically the deformity is seen as a wedge depression. It is considered that this indicates normal healing and a safe scar. Any irregularity in the deformity, however, indicates a weak scar and the advisability of Caesarean section rather than vaginal delivery in the event of a future pregnancy.

The author suggests that the raised blood corticosteroid levels of pregnancy may play a part in the defective union of some Caesarean section wounds of the uterus.

R. W. Grayburn

MATERNAL MORBIDITY

113. **Treatment of Puerperal Mastitis.** (Considerazioni sulla terapia delle mastiti puerperali.)

By E. FERRARIO and S. MANGIAMELLI. *Minerva ginec. Torino*, **11**, 857–864. Oct. 31, 1959. 30 charts. 3 refs.

Staphylococci unaffected by penicillin and sulphonamides and resistant to streptomycin are frequently found in cases of puerperal mastitis, and such cases may go on to suppuration in spite of treatment with these antibiotics. Moreover, whilst it is highly inadvisable to give these remedies prophylactically (under the so-called antibiotic umbrella), it is equally desirable to start treatment as soon as possible after the first signs of mastitis appear. The diagnostic method advocated is to culture the breast milk against sensitivity testing, which procedure in their experience always gives a prompt and correct answer. The antibiotic they have found almost universally acceptable for mastitis is spiramycin.

W. C. Spackman

INFANT

114. **Urinary Infection in the Newborn.**
By U. JAMES. *Lancet*, **2**, 1001–1002. Dec. 5, 1959.

The author draws attention to the difficulties in diagnosing urinary infection in newborn infants and emphasizes the need to examine the urine of any infant with unexplained loss of weight, failure to gain weight, apathy or anorexia.

In a preliminary investigation it was found that uncentrifuged urine from normal female infants contains less than 50 white cells per c.mm. and from normal male infants less than 25 white cells per c.mm. By this means the diagnosis of urinary infection was made in 32 infants aged between 6 and 12 days, an incidence of 1·5 per cent of all live births in the period under review. The diagnosis was confirmed by a positive culture in every case.

The majority of the babies were treated with sulphonamide (sulphadimidine or "sulphatriad") in doses of 1 g. daily for 14 days followed by a further course of 0·25 g. for 4 weeks. The importance of prolonged treatment in preventing recurrence of the infection is emphasized and the author recommends that supervision be continued for a number of years so that any associated congenital abnormalities of the renal tract may be detected.

J. M. Brudenell

115. **Causes and Treatment of Asphyxia Neonatorum.** (Ursachen und Behandlung des Neugeborenenscheintodes.)
By K. SCHLAGETTER. *Zbl. Gynäk.*, **81**, 1756–1765. Oct. 31, 1959. 4 figs. 39 refs.

The author discusses the physio-pathology of asphyxia of the newborn. He points out that anaemia, either acute or chronic, due to haemorrhage, placental pooling of blood, haemolysis or infection, may at times be responsible for asphyxia. In cases of acute blood loss haemoglobin estimation may not help in the diagnosis. He considers, therefore, that a transfusion of 20 ml. of blood per kg. of body-weight should be given to those cases of peripheral disturbance of respiration in which oxygen, circulatory stimulants and i.v. dextrose failed to improve the condition of the child. He draws up a scheme of resuscitation in steps to be taken in the following order if applicable: (1) respiratory difficulty due to peripheral causes is treated by aspiration of the respiratory passages and supply of oxygen; (2) central (C.N.S.) respiratory failure is treated by artificial endotracheal positive pressure, administration of oxygen and possibly analeptic drugs; (3) circulatory failure is dealt with by intravenous injection of dilute circulatory stimulants: 0·003 g. of lobeline in 10 ml. of 10 per cent dextrose solution, given in successive doses of 2 ml. at a time; noradrenaline may be used in addition, if necessary. (4) In cases of oligaemic shock intravenous dextrose or saline is given by cannula through the umbilical vein. (5) Anaemia is treated by blood transfusion.

The author recommends the "blind" endotracheal intubation as an expedient and satisfactory technique, particularly when laryngoscopes are not available. The larynx is identified with the index finger and the endotracheal tube is guided alongside it.

Bruce Eton

116. **The Case for Conservatism in Management of Foetal Distress.**
By N. WALKER. *Brit. med. J.*, **2**, 1221–1226. Dec. 5, 1959. 23 refs.

Foetal distress occurred in 700 (5·5 per cent) of 12,000 confinements at King Edward VIII Hospital, Durban. These 700 cases were studied in two equal groups. The first 350 cases were delivered by various obstetricians, some radical and some conservative in their management of foetal distress. Experience gained in this preliminary survey led to a controlled study of 350 cases, the management of which—intervention or non-intervention—was determined by drawing a sealed envelope from a drum. Strict control was impossible because in 36 "non-intervention" cases an operative delivery was necessary for reasons other than foetal distress and 68 of the "intervention" cases delivered spontaneously very soon after distress became manifest. Cases of breech presentation and prolapsed cord were excluded.

The perinatal loss in the non-intervention group was 6·8 per cent and that in the intervention group was 8 per cent.

It appeared, therefore, that in the absence of any complication such as prolapse of the cord "a policy of non-intervention is not necessarily fraught with dire consequences", and the author concludes that "the onset of distress should be an indication to search for the cause rather than a demand for dramatic action".

This study also suggested that whereas meconium staining of the liquor is a definite sign of foetal distress, the behaviour of the foetal heart is of doubtful value in assessing the condition of the foetus *in utero*.

R. W. Grayburn

117. **Maori Infant Mortality.**
By C. E. GARDINER. *N.Z. med. J.*, **58**, 321–340. June 1959. 38 tables.

The Maori infant mortality rate has been extraordinarily high until very recently, when a great improvement occurred. The rate in 1958 was 54·37 per thousand live births. The European rate in the same year was 19·40 per thousand live births. The overall improvement in the Maori rate that has taken place in the last few years is relatively greater than that achieved with the European rate. The Maori death rates are much higher than the European for respiratory and gastric and intestinal diseases. These disorders cause the greatest loss of infant life after the first month of life, and can be caused by environment, housing and sanitary conditions, and lack of medical and nursing care. In deaths under one month the European rate per thousand live births was 13·88, while the Maori rate was 20·45. In deaths from 1–12 months, the European rate was 5·89, while the Maori rate was 37·10. A special survey was made of Maori households in certain districts to study the possible influence of the environment on the high Maori infant mortality.

This paper records the medical and nursing care during pregnancy and after delivery, and the frequency of consultations during the first year of infant life. It also records details on the dwellings and amenities of the Maoris. The tables are given in great detail and relate the infant mortality with the housing and sanitary conditions. This paper is one of great interest from the sociological and preventive medicine aspects.

L. Woodrow Cox

GYNAECOLOGY

118. **The Squamocolumnar Transitional Zone of the Cervix Uteri.**

By C. F. FLUHMANN. *Obstet. Gynec.*, **14**, 133–148. Aug. 1959. 11 figs. 17 refs.

The squamocolumnar transitional zone of the cervix was studied in 267 histological sections. Of these, 155 were from adult women; 40 during pregnancy, 23 two years or more after the menopause, and 49 from babies and children. In only 29 per cent was the classic picture seen of an abrupt change from the fully differentiated squamous epithelium of the portio vaginalis to the columnar epithelium of the cervical canal. In 71 per cent there was a zone of transition between the two. This transitional zone measured between 1 and 10 mm. in width, and within these areas there was an intense leukocytic infiltration. The epithelium in the zones is composed of groups of immature cells evolving into squamous epithelium. The term "squamous prosoplasia" has been used to describe the process.

It seems that the squamocolumnar zone is not a static structure, but that the epithelium is constantly undergoing a process of disintegration and regeneration which is accompanied by an inflammatory reaction.

J. G. Dumoulin

119. **Histidine in Gynaecological Treatment.** (Histidina in terapeutica ginecologia.)

By E. STREJA. *Obstet. Ginec.* (*Bucarest*), pp. 511–516. Nov. 1958. 8 refs.

Many gynaecological disorders are due to imbalance of the hypothalamus-pituitary-ovarian system. The initial fault may be in hypothalamus, pituitary or ovary, but the final result is hyperoestrinism. The clinical manifestations may be (1) pelvic congestion or breast engorgement, (2) allergic, (3) neuro-vegetative, (4) psychological and (5) water retention. Not only oestrogens, but other ovarian hormones may be produced in excess. Stimulation of the hypothalamus liberates acetylcholine, which influences the hypersecretion of the ovary, hence the excessive oestrogenic effect on the genital tract. The ultimate effect is due to acetylcholine alone, or in synergism with adrenaline. Excess of progesterone finally produces histamine.

The author has treated 30 cases of a variety of hormonal disorders, including 12 with pelvic congestion (pre-menstrual, dysmenorrhoea and irregular bleeding), 4 cases with polycystic disease of the ovaries, 4 psychoneurotic cases, 3 cases of pre-menstrual breast engorgement, and 7 cases of severe mycotic vaginitis of hyperoestrogenic origin. He used histidine, which has anti-acetylcholine and anti-histamine properties to block the acetylcholine function of the F.S.H. and oestrogen, as well as the acetylcholine function of L.H., L.T.H. and progesterone.

Spectacular results are claimed. After continuing the treatment in each menstrual cycle for a few months the disturbances were suppressed, and in some cases did not recur. It is claimed that treatment with histidine can replace other hormonal treatment.

Sylvia Lerer

120. **Menstrual Disturbances in Genital Tuberculosis.** (Die Menstruationsstörungen bei der Genitaltuberkulose.)

By V. D. PETRESCU and H. CONDREA. *Zbl. Gynäk.*, **81**, 1791–1801. Nov. 7, 1959. 6 tables. 18 refs.

The authors investigated the effects of proved genital tuberculosis on menstrual function in a series of 115 patients. The behaviour of the periods was studied before and one year after treatment was begun.

Disorders of menstruation were observed in 80 per cent of the cases. Amenorrhoea was present in 22·6 per cent. Amongst 70 patients treated medically periods were scanty in 10 per cent, irregular in 14·2 per cent, heavy or frequent in 25·8 per cent and normal in 22·9 per cent. One year after beginning treatment the periods had become normal in 51·5 per cent, irregular in 14·2 per cent, scanty in 14·2 per cent, heavy or frequent in 5·8 per cent and amenorrhoea occurred in 14·3 per cent.

Comparison between the 70 cases treated medically and 36 cases who underwent surgical treatment showed that amongst the former (with comparatively minor lesions) amenorrhoea was slightly more common, whereas menorrhagia was seen more often in the latter patients (with more extensive disease of the genital organs).

As regards the cases of amenorrhoea, the authors found that the chance of restoring menstrual function decreased with the duration of the amenorrhoea before treatment was begun. Thus the two factors, duration and extent of the disease, are of considerable importance from the point of view of prognosis, particularly in cases of primary amenorrhoea. Early diagnosis and treatment are therefore emphasized.

The authors discuss the possible mechanisms by which menstrual function is deranged in cases of genital tuberculosis: (1) neuro-humoral reflexes started by the inflammatory process; (2) changes in the endometrium with formation of intra-uterine adhesions; (3) the action of tuberculous toxins irrespective of the size of the morphological lesions, as is classically seen in cases of pulmonary tuberculosis with amenorrhoea. As the majority of cases of primary amenorrhoea in the authors' series were associated with genital tuberculosis of limited extent (absence of palpable structural abnormality), the conclusion is drawn that the amenorrhoea in these cases is caused by a toxic effect of the tuberculous process blocking ovarian function.

Bruce Eton

NEW GROWTHS OF THE REPRODUCTIVE ORGANS

121. **Methods and Results in a Tumour Detection Clinic.** (Methoden und Ergebnisse einer Geschwulstberatungsstelle.)

By G. Waschke, M. Schwartz and H. K. Marx. *Zbl. Gynäk.*, **81**, 1670–1680. Oct. 17, 1959. 1 table. 6 figs.

On the suggestion of the local health authority a free service for the detection of tumours amongst women was established in the Spandau area of Berlin. The female population was encouraged by circulars and public talks to attend for examination. During the initial weeks 60–80 women attended per session and in the subsequent years 1950–1957 an average of 20–30 women. A total of 5,905 women were examined. Routine investigation included physical, cytological and colposcopic examination.

Five hundred and twenty-four were symptom free, but 52 of them had an abnormality of the breast or genital tract requiring treatment. Treatment was also required for disorders of the genital tract by 175 out of 1,502 women complaining of backache; by 230 out of 1,713 complaining of lower abdominal pain; by 171 out of 1,529 complaining of vaginal discharge; and by 15 women out of 304 with vague general symptoms. In addition, there were many women complaining of dyspareunia, menorrhagia, breast symptoms, constipation and disorders of micturition.

Seven hundred and sixty-nine women complained of symptoms which are generally regarded as suspicious of a neoplasm in the genital tract, which was present in 76 of them. Amongst the remaining 5,136 women who had no such symptoms, a cancer was found in only 29.

Twenty-six women had an acute inflammation of the adnexa or parametrium; 222 had chronic adnexal inflammation, 70 were pregnant, 31 had cysts or fibromata in the vulva or vagina, 40 had simple ovarian cysts, 70 had ovarian tumours, and 187 had uterine fibroids. There were 18 cases of intra-epithelial carcinoma of the cervix, 12 micro-carcinomata of the cervix, 4 carcinomata of the corpus uteri, 4 of the ovary, 2 of the vulva, 1 of the vagina and 2 of the uterine tubes. Furthermore, 3 carcinomata of the rectum were detected.

Altogether there were 87 cases of carcinoma amongst the 5,905 women (1·47 per cent).

A follow-up study of 3 cases of untreated intra-epithelial cancer of the cervix is included. *Bruce Eton*

122. **Myomectomy: Follow-up Results.** (La miomectomia. Ricerca clinico-statistica sui suoi esiti a distanza in rapporto alle funzioni genitali.)

By P. C. Pozzi and M. Rubbiani. *Minerva ginec., Torino*, **11**, 676–678. Aug. 31, 1959. 4 tables. 54 refs.

In a ten-year review (1945–54) at Milan, 1,333 cases of uterine fibroids were treated by total or subtotal hysterectomy and 175 by myomectomy. Of the latter, a follow-up was possible in 138. In 68 per cent of these menstruation was regular and normal. Thirty per cent had had successful pregnancies whilst 70 per cent had either remained sterile or had aborted. Of the 38 successful pregnancies, 27 had normal deliveries, whilst 5 required forceps and 6 Caesarean section. Clearly, myomectomy should be resorted to in women of child-bearing age unless other considerations contra-indicate it.

W. C. Spackman

123. **Report of a Diagnostic Centre for Uterine Carcinoma.** (Rilievi clinico-statistici su 2,250 esami colposcopici e cito-cariologici eseguiti presso il Centro per la diagnosi e profilassi dei tumori genitali feminili della Clinica Ostetrico-gineologica di Perugia.)

By T. Baçal and P. Palazzetti. *Minerva ginec., Torino*, **11**, 943–948. Nov. 30, 1959. 7 tables. 1 fig. 12 refs.

The centre is an out-patient clinic fully equipped for colposcopic and laboratory diagnosis, including cytokaryology and histopathology. It is not stated whether patients are referred to it or come of their own initiative. No fees are charged. After a full history has been recorded a general colposcopic examination is made when, after a preliminary test for trichomonas, etc., on a fresh preparation, the cervix is treated with 3 per cent acetic acid and a full Hinselmann colposcopy of the vagina and cervix is carried out, including inspection with the aid of Kogan's divaricator of the first centimetre of the cervical canal. At the same time slides are taken for cytological and karyological examination after appropriate staining. The colposcope enables accurate "aimed" biopsy to be undertaken of specially suspicious spots. Schiller's test is found of value in selecting such spots, other characteristics of which are leucoplakia, rough stratified patches, raised depressed or friable areas, or irregularity of visible blood vessels.

Results: 2,250 complete examinations were made, involving 198 "aimed" biopsies of which 19 were positive for carcinoma, 10 being intra-epithelial. The total number of carcinomas found was 53 of which 33 were diagnosable clinically and the remainder might have escaped diagnosis.

Whilst affirming the value of colposcopy as indicated above, emphasis is laid on the special usefulness of cytology. Malignant tissues desquamate even more freely than does the normal genital tract, and as endocervical carcinoma is difficult to diagnose with the colposcope, a light curettage of the endo-cervix is advised for the cytokaryological test. In fact this centre has found it essential to submit all cases to both methods, as occasional cases would have been missed by each used alone, and false negatives occurred with either, and indeed with both combined.

W. C. Spackman

124. **Methotrexate in Treatment of Metastasizing Choriocarcinoma.**

By A. E. R. Buckle. *Brit. med. J.*, **2**, 1210–1213. Dec. 5, 1959. 6 figs. 8 refs.

A case of metastasizing chorioncarcinoma treated with methotrexate and 6-mercaptopurine is described and the medical literature is reviewed.

The case, though fatal, is reported in the hope that

interest may be aroused in this form of therapy which may be of value in advanced disease.

R. W. Grayburn

125. **Dysgerminoma. Report of a Case Treated by Surgery and X-ray Therapy and Followed by Term Pregnancy.**

By R. I. AYERST and C. G. JOHNSON. *Obstet. and Gynec.*, **14**, 685–687. Nov. 1959. 12 refs.

In 1944 the patient whose history is given had her right ovary removed at the age of 18. At the time the left ovary looked normal. The diagnosis of the cystic right ovary was dysgerminoma. Because of the potential danger of malignancy, deep X-ray treatment was given to the left ovary. The patient had amenorrhoea for 2½ years. In 1958 she had a normal pregnancy and produced a healthy infant.

The authors add that, notwithstanding this case, in their opinion total hysterectomy and bilateral salpingo-oöphorectomy followed by X-ray therapy is the procedure of choice for dysgerminoma regardless of age and parity.

J. G. Dumoulin

126. **Effects of Progestin-Induced Pseudopregnancy on Endometriosis: Clinical and Microscopic Studies.**

By M. C. ANDREWS, W. C. ANDREWS and A. F. STRAUSS. *Amer. J. Obstet. Gynec.*, **78**, 776–783. Oct. 1959. 2 tables. 3 figs. 6 refs.

Because of the frequent improvement in endometriosis following pregnancy, the authors produced pseudo-pregnancy in 24 patients. Enavid (19 norethinordrel with 1·5 per cent ethinyl-3, methyl-, estradiol ether; G. D. Searle & Co.) was used, 10 mg. being given daily for 10 days, then 20 mg. daily for 2 weeks, and then 30 mg. daily for the period of treatment—14 to 22 weeks. There was a marked decidual response in all. The uterus usually enlarged to twice the normal size during treatment, and became softer, and returned to normal size and consistency afterwards. Pain was much diminished or entirely absent during treatment, and tenderness in utero-sacral nodules was diminished or eliminated. Follow up for 1 to 11 months indicated that the improvement usually persisted, especially if the pseudopregnancy was maintained for 20 weeks or longer. At present the method seems particularly useful (1) in fresh increasingly severe cases of endometriosis in young women whose future reproductive function may be important and (2) in recurrent endometriosis after conservative operations in young women.

F. J. Browne

127. **Invasive Carcinoma of the Cervix in New Zealand.**

By H. M. CAREY and C. E. GARDINER. *N.Z. med. J.*, **58**, 341–355. June 1959. 20 tables. 1 fig. 3 refs.

Since 1948 details of almost all cases of carcinoma of the cervix in the population of New Zealand have been available for study. In 1948 a National Cancer Register was set up and it has been obligatory for all public hospitals to report all cases of carcinoma. In the centres where facilities exist for the treatment of carcinoma of the cervix in private hospitals the gynaecological specialists have been contacted personally and have co-operated in supplying details to the Register. Statistics are presented showing the incidence per year in the population for various age groups, and the incidence of cases at each stage of carcinoma of the cervix for each age group. The higher incidence occurs at ages 55–59. The treatment given is also recorded, and the five-year survival rates. In Stage I this was 68·3 per cent, Stage II 39·4 per cent, Stage III 12·0 per cent, Stage IV 2·0 per cent. The survival for all stages was 39·5 per cent.

The results of treatment with radium, radium plus deep X-ray, radical surgery with or without radiotherapy are recorded. There seems to be very little difference in the results obtained with radium alone and where radium plus deep X-ray was used. The number of cases in this series where radical surgery was used as the treatment of choice is comparatively small, and the results are similar to the results using radium.

L. Woodrow Cox

OPERATIONS

128. **Hysterosalpingography with a New Water-Soluble Medium. Diatrizoate Iodipamide Methylglucamine.**

By W. J. SWEENEY. *Obstet. and Gynec.*, **14**, 677–683. Nov. 1959. 6 figs. 22 refs.

The author tested a new water-soluble medium, Sinografin, made by the Squibb Institute for Medical Research, in 100 hysterosalpingograms. The medium was found to be non-irritating and non-toxic, producing no side effects. The quality of the radio-opacity obtained was excellent. Only 1·5 ml. of dye was sufficient to fill even the largest uterus and a small number of X-ray exposures gave accurate diagnosis.

J. G. Dumoulin

129. **The Results of Cysto-Urethrographic Selection of Patients with Stress Incontinence for Operative Treatment.** (Die Resultate einer urethrozystographisch differenzierten operativen Behandlung der Stress-Inkontinenz.)

By J. JANSSENS. *Geburtsh. u. Frauenheilk.*, **19**, 992–1002. Nov. 1959. 3 tables. 6 figs. 40 refs.

The author has used pre- and post-operative urethro-cystograms to determine the indications for and to assess the results of different operations for stress incontinence in the University Gynaecological Clinic of Groningen. Before such studies were made 253 patients were operated on vaginally and 65 per cent were cured of their stress incontinence. Using urethro-cystograms patients with stress incontinence were divided into two groups, those with loss of the posterior urethro-vesical angle (type A) and those with herniation of the bladder base but with little or no distortion of the posterior urethro-vesical angle (type B). In 26 patients with a urethro-cystogram of type A a vaginal repair was performed; 16 (61 per cent) were cured of stress incontinence. In a later series a group of 106 patients belonging to type A were treated by means of a Marshall-Marchetti

(modified by Ten Berge) operation; 91 (86 per cent) of these were cured. Another group of 14 patients with urethro-cystograms of type B were treated for stress incontinence by vaginal repair and of them 12 (86 per cent) were cured.

Peter J. Huntingford

130. **Urinary Fistulae in Women, with Special Reference to Their Operative Technique.**

By H. M. LAZARUS. *J. Obstet. Gynaec. India*, **10**, 1–11. Sept. 1959. 5 tables. 6 figs. 4 refs.

The type of Indian woman who presents herself for the relief of her vesico-vaginal fistula, is described as feeble, anaemic, malaria-stricken, under-nourished, and infested with hook worms and round worms. Her prolonged labours are attended by untrained handy women, and end in stillbirths, with urinary and faecal fistulae. Two hundred and forty-two such women were operated upon over a 10-year period. Of these, 95 per cent had fistulae due to obstetric trauma, the great majority being non-instrumental deliveries.

Pre-operatively the patient's general condition is built up, particular care being taken to treat ascaris lumbricoides which may work its way into the vagina, and interfere with the sutures. Operation is advised three months post-partum.

The Trendelenburg-lithotomy position is used, with a Schuchardt's incision. The latter is frequently repaired by employing a piece of mucous membrane from a patient of the same blood group. Long-handled light instruments, and fish-hook needles are used. When the antero-lateral part of the bladder wall close behind the symphysis pubis is destroyed a symphysiotomy or pubiotomy is done to facilitate mobilization of the bladder. In a generally contracted pelvis a bone graft has been done, taking a wedge from the tibia, and embedding it between the pubic rami to enlarge the pelvic brim.

The flap-splitting operation is usually employed. Two continuous No. 00 chromic catgut stitches are used for the bladder wall, avoiding the mucosa, and the vaginal epithelium is closed with interrupted No. 1 catgut. Any recto-vaginal fistula which may be present is closed at the same time. Openings into the urethra are closed in the same way as the bladder fistula. Post-operatively a catheter is kept in the bladder for nine days, and urinary antiseptics are employed before and after operation. The patient is kept constipated for five days.

The patient is advised to have any subsequent confinement in hospital, but is not necessarily treated by Caesarean section.

John McKiddie

131. **Hysterotomy Scars in the Region of the Isthmus Uteri.** (Über Hysterotomienarben in der Zervix-Isthmus-Wand.)

By J. LINDAHL and C.-G. HELANDER. *Geburtsh. u. Frauenheilk.*, **19**, 959–966. Nov. 1959. 4 tables. 39 refs.

The authors have studied by means of hysterosalpingograms in 479 patients the uterine scars resulting from vaginal hysterotomies performed in the Karolinska Sjukhuset, Stockholm, for termination of pregnancy. The uterus was emptied, after displacement of the bladder, through a longitudinal incision of 4–5 cm., in the anterior wall of the isthmus uteri just above the cervix. The hysterosalpingograms were performed 1–3 years after the hysterotomies.

In 127 patients the X-rays showed a funnel-shaped depression in the anterior wall of the uterus in the region of the scar. The authors have correlated this appearance of "scar hernia" with various factors in the patient's history. There was no relationship between "scar herniation" and the time in pregnancy that the termination was performed. The deformity was noted twice as often in primigravidae as in multiparae. Post-operative infection of the genital tract increased the incidence of "scar weakness". The operations were performed by several different surgeons, some of whom closed the uterine wound with very closely placed interrupted catgut sutures, others used fewer and more widely spaced sutures of the same material. There was no correlation between the incidence of "scar hernias" and the technique used for closing the uterus. The authors relate the greater incidence of "scar hernia" in primigravidae to the increased difficulty of performing vaginal hysterotomy in such patients.

[The X-ray appearances, described in this article, of the uterine scar following vaginal hysterotomy are the same as those to be found following lower segment Caesarean section as described by Poidevin and Bockner (*J. Obstet. Gynaec. Brit. Emp.*, 1959, **65**, 278). These authors were, however, unable to relate the deformity of the scar to parity, operative technique or the incidence of post-operative infection. In a later paper Poidevin (*Brit. med. J.*, 1959, **2**, 1058), has indicated that wedge-shaped deformities, up to 5 mm. in depth, in the region of the scar may be considered as normal; and that only large irregular deformities should be considered the result of pathological healing. Even although the incisions in the two series were made in different directions, the outcome of any subsequent pregnancies in the group of Swedish patients will be of interest, especially with regard to the strength of the scars, which showed the deformity described.]

Peter J. Huntingford

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